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IN THE

Supreme Court of the United States

DAIICHI SANKYO CO., LTD. and
DAIICHI SANKYO, INC.,
Petitioners,

v.

APOTEX, INC. and APOTEX CORP.,
Respondents.

On Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

PETITION FOR A WRIT OF CERTIORARI

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QUESTIONS PRESENTED

1. Whether the Federal Circuit, in the aftermath of this Court's decision last term in *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007), has adopted an overbroad concept of obviousness, labelling a patented invention obvious when, at most, the prior art suggested it was a method "obvious to try."

2. Whether the Federal Circuit, in adopting an overbroad concept of obviousness, wrongly relied on the education, skill, and experience of the inventors themselves in describing the hypothetical "person having ordinary skill in the art."

RULE 29.6 CORPORATE DISCLOSURE STATEMENT

Daiichi Sankyo Co., Ltd. is not owned by a parent corporation and no publicly held company owns 10% or more of its stock. Daiichi Sankyo, Inc. is a subsidiary of Daiichi Sankyo Co., Ltd.

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On Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

PETITION FOR A WRIT OF CERTIORARI

Petitioners, by their undersigned counsel, respectfully petition for a writ of certiorari to review the judgment of the United States Court of Appeals for the Federal Circuit in this case.

OPINIONS BELOW

The court of appeals' opinion (App. A) is reported at 501 F.3d 1254. The district court's opinion granting judgment for petitioners (App. B) is reported at 441 F. Supp. 2d 672. The district court's claim construction opinion (App. C) is reported at 380 F. Supp. 2d 478.

JURISDICTION

The judgment of the court of appeals was entered on July 11, 2007. A timely petition for rehearing was

denied on September 11, 2007. App. D. The jurisdiction of this Court is invoked under 28 U.S.C. § 1254(1).

STATUTORY PROVISION INVOLVED

35 U.S.C. § 103(a) provides:

> A patent may not be obtained . . . if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

STATEMENT OF THE CASE

A. Introduction

This case involves a patented method for using the antibiotic ofloxacin in topical form, *e.g.*, in an ear drop solution, to treat bacterial ear infections. The Federal Circuit held the patent invalid for obviousness, despite the contrary conclusion reached by the district court after a nine-day bench trial.

The Federal Circuit made three principal errors in reaching this result. First, it wrongly relied on the benefits of hindsight in 2007 to decide what would have been obvious to a person of ordinary skill in the art on April 8, 1988, the priority date of the patent-in-suit. On this basis, the court disregarded numerous indicators of non-obviousness, such as satisfaction of a long-felt medical need, unexpected results, extensive industry recognition, and commercial success. Second, the court unilaterally adopted its own description of a hypothetical person

of ordinary skill in the art, rejecting the district court's common-sense approach and wrongly relying on the inventors' own skill, education, and experience. Third, the court focused incorrectly on the compound ofloxacin itself, rather than the patented *method* of using ofloxacin in an ear drop solution that could be applied directly into the ear (rather than being administered as a pill, by injection, or in some other systemic form).

Review by this Court is needed to rectify the court of appeals' overly broad application of obviousness as a basis for invalidating a successful invention and patented method of treatment, achieved only after extensive research and testing regarding whether a direct, topical application method could be used safely and effectively in the ear.

B. Background

Petitioner Daiichi Sankyo Co., Ltd. is a pharmaceutical company that owns the patent-in-suit, U.S. Patent No. 5,401,741, entitled "Topical Method for the Treatment of Otopathy" ("the '741 patent"). The company also holds an FDA-approved New Drug Application ("NDA") for a commercial product, FLOXIN® Otic (Ofloxacin Otic Solution, 0.3%), that is intended for topical application into the ear for the treatment of bacterial ear infections, as the '741 patent teaches. App. 2a-3a, 15a. Petitioner Daiichi Sankyo, Inc. is a subsidiary of Daiichi Sankyo Co., Ltd. and is the exclusive marketing agent for FLOXIN® Otic in the United States. We refer to petitioners together as "Daiichi."

The compound ofloxacin was patented in May 1983, and the inventors assigned their patent rights to

Daiichi. App. 18a n.8; A. 11269-76.[1] The '741 treatment method was patented in March 1995. The inventors of the '741 patent—a medical school professor and two Daiichi employees—also assigned their patent rights to Daiichi. App. 5a-6a, 15a.

The '741 patent is a treatment method patent. It marked an advance in the manner of treating bacterial ear infections by using direct, topical administration of the antibiotic compound ofloxacin. Before the '741 patented invention, all of the available antibiotic ear drops for the treatment of bacterial ear infections were potentially "ototoxic" at prescribed doses. That is, they had a propensity to cause hearing impairment, by damaging the cochlea and its hair cells, or balance impairment, by damaging the vestibular system of the inner ear. App. 19a-20a. If the ear drum (*i.e.*, the tympanic membrane) were perforated, antibiotics administered in the external auditory canal could enter the middle ear space and migrate to the inner ear, where they could cause the kind of cochlear or vestibular damage just mentioned. As a consequence, the FDA prohibited the use of antibiotic ear drops to treat ear infections where it was known or suspected that the ear drum was not intact. Moreover, because of the swelling, inflammation, discharge, and pain frequently associated with ear infections, the status of the ear drum could be difficult to determine. The FDA therefore urged caution in the use of antibiotic ear drops even in the treatment of infections in the external auditory canal. App. 20a-21a.

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[1] "A." refers to the Joint Appendix in the court of appeals.

C. The '741 Patented Invention

In 1986-87, the inventors of the '741 patent conducted a research program to develop a new method of treating bacterial ear infections through the topical administration of ofloxacin into the ear. Because of the safety issues described above, the inventors devoted substantial time and resources to extensive testing of ofloxacin solution on animals (guinea pigs). They demonstrated that a 0.3%-0.5% ofloxacin solution, even when applied directly into the middle ear space, did not have any significant adverse effect on hearing and did not otherwise harm the animal's cochlear hair cells. App. 22a-23a. The testing further showed that the ofloxacin remained present at the targeted site of the infection in sufficient concentration and for an extended period of time (up to several hours) so as to inhibit or kill the bacteria at issue without migrating to any significant extent elsewhere in the animals' system. App. 23a-24a. This latter research result was significant because ofloxacin administered systemically for absorption into the bloodstream (*e.g.*, through a pill or injection) was known to affect adversely the weight-bearing joints of young animals. The drug, therefore, was never approved for systemic use in pediatric patients in the United States or Japan. A. 5938. Moreover, use of systemic antibiotics generally raised concern about undesirable consequences, including development of bacterial resistance and side effects such as diarrhea, vomiting, and allergic reactions. App. 21a.

On March 28, 1995, Daiichi obtained the '741 patent for the use of topically administered ofloxacin to treat bacterial ear infections. In December 1997,

the FDA approved Daiichi's NDA for FLOXIN® Otic, and Daiichi began marketing its product. App. 15a. FLOXIN® Otic is the first antibiotic ear drop medicine ever approved by the FDA for use in patients with a perforated or ruptured eardrum. App. 19a, 63a; A. 6142.

D. The Apotex ANDA

Sometime in early 2000, around the time when the patent on the ofloxacin compound expired, respondents Apotex, Inc. and Apotex Corp. (affiliated companies referred to collectively as "Apotex") began the process of preparing a generic ofloxacin otic solution identical to Daiichi's FLOXIN® Otic. App. 25a. In October 2002, Apotex submitted an Abbreviated New Drug Application ("ANDA") to the FDA, seeking approval to market and sell the generic version of Daiichi's FLOXIN® Otic in the United States for the same ear infections for which Daiichi's product was previously approved. App. 26a. Apotex's ANDA included a "Paragraph IV Certification" challenging the validity of Daiichi's '741 patent, and Apotex undertook to provide the statutorily required notice to Daiichi. Daiichi received the required notice of Apotex's ANDA in February 2003. App. 16a-17a, 63a; A. 8095.

E. The District Court's Decision

In March 2003, Daiichi filed this action in the United States District Court for the District of New Jersey. A. 105. Daiichi alleged that Apotex, by filing and seeking approval of its ANDA, infringed the '741 patent, in violation of 35 U.S.C. § 271(e). Daiichi further alleged that Apotex's proposed manufacture, marketing, and sale of a generic 0.3% ofloxacin otic

solution during the term of the '741 patent would infringe the patent, in violation of 35 U.S.C. § 271(a), (b), or (c). A. 759-64.

In August 2005, following a hearing under *Markman v. Westview Instruments, Inc.*, 517 U.S. 370 (1996), the district court construed disputed terms in the claims of the '741 patent. Relying on settled Federal Circuit law, the court gave the claim terms their "ordinary and customary meaning," *i.e.*, the meaning that the terms would have had to "a person of ordinary skill in the art in question at the time of the invention . . . ." App. 65a; *see Phillips v. AWH Corp.*, 415 F.3d 1303, 1311 (Fed. Cir. 2005). It was in this context—construing the terms used in the patent, *not* addressing Apotex's obviousness defense—that the district court determined that the person of ordinary skill in the art would be a person with a medical degree (*e.g.*, a pediatrician or general practitioner) and experience treating patients suffering from ear infections and with basic knowledge of the pharmacology and use of antibiotics. App. 69a-70a. Viewing the claim terms from this perspective, the district court construed "otopathy" to mean "bacterial ear infection," and it construed the phrase "effective to treat" to mean "efficacious and safe." App. 76a, 77a. The court included a safety component in this construction because, as the development of the '741 invention demonstrated, safety (and, in particular, the reduction or avoidance of ototoxicity) was a paramount concern of the inventors. App. 76a-77a.

The district court conducted a nine-day bench trial in November 2005. App. 12a n.1. Shortly before trial, Apotex stipulated that the method of treating bacterial ear infections by administering a generic ofloxacin otic solution, 0.3% for which Apotex sought

approval in its ANDA fell within the scope of several of Daiichi's claims in the '741 patent. App. 54a; A. 10947-49. Accordingly, as the case went to trial, there was no remaining issue as to infringement, and the only matters to be decided were Apotex's defenses of patent invalidity based on alleged anticipation and obviousness, and patent unenforceability based on inequitable conduct.

The district court rejected Apotex's claims of patent invalidity and unenforceability and entered judgment for Daiichi. App. 56a-58a. Of greatest relevance now in light of the court of appeals' subsequent decision, the district court rejected Apotex's contention that the '741 invention was obvious in light of the prior art. Apotex cited four earlier patents and three articles in support of its obviousness argument. The district court carefully reviewed each of them and provided a detailed explanation for why they did not render the '741 patented invention obvious. App. 37a-46a.

For example, none of the four earlier patents involved any disclosure of the safety of ofloxacin when topically applied in the ear. One of the articles discussed a clinical study to evaluate the efficacy and safety of ofloxacin when administered *orally* to treat middle ear infections. A second article by the same author (actually a later version of the first) concluded by suggesting that eardrops containing ofloxacin should be *tested* for efficacy and possible ototoxicity. As the district court found, a person ordinarily skilled in the art would not conclude from the article that "topically administered ofloxacin would be safe to treat bacterial ear infections." App. 43a. At most, a person ordinarily skilled in the art would learn that

"topically administered ofloxacin to the ear must be tested to determine its safety." *Id.*

Finally, the district court considered the so-called Ganz article, published in German with an English abstract. App. 44a-46a. The article discussed not ofloxacin but another antibiotic known as ciprofloxacin. Ciprofloxacin and ofloxacin are both members of a large group of antibiotics known as gyrase inhibitors. The Ganz article reported some success in treating chronic bacterial ear infections with a ciprofloxacin solution, but it also reported that gyrase inhibitors were "antibiotics of second choice" and that for local treatment in the ear gyrase inhibitors "should be used only in difficult cases and exclusively by the otologist." App. 44a. The district court found on this basis that the Ganz article actually "teaches away" from the '741 patent and does not support the argument that a person ordinarily skilled in the art would know that topical use of ofloxacin to treat bacterial infections is both efficacious and safe. *Id.*

In rejecting Apotex's obviousness claim, the district court also relied on several "secondary considerations." The court found, for example, that the '741 patent "satisfied a long-felt medical need by providing physicians with a nonototoxic alternative to the available drugs to treat bacterial ear infections." App. 46a n.25. The '741 patent also did not cause the same safety concerns of side effects, bacterial resistance, irritation of the middle ear mucosa, and concentration of the drug absorbed in the blood stream, central nervous system, and inner ear perilymph as did conventionally available antibiotics. *Id.* The court further found that Daiichi's FLOXIN® Otic product was commercially

successful, increasing its market share to 20% within the first five years at the expense of branded and generic competitors. *Id.* It specifically found that a competing product called Cortisporin® Otic, which was well-established in the marketplace, lost significant market share after FLOXIN® Otic was introduced. *Id.*

For all these reasons, the district court concluded that the '741 patent was not invalid for obviousness.

F. The Court of Appeals' Decision

The Federal Circuit reversed and held the '741 patent invalid as obvious. App. 1a-10a. The court proceeded in two steps.

First, the court of appeals criticized the district court's description of a person having ordinary skill in the art. App. 4a-6a. The court made this discussion a centerpiece of its opinion, even though the district court, in finding nonobviousness, simply addressed the prior art itself and what it did and did not disclose. In rejecting Apotex's claim of obviousness, the district court did not rely on, or tilt in Daiichi's favor because of, the court's ruling a year earlier, in the claim construction opinion, about the characteristics of a person having ordinary skill in the art.

Nonetheless, the Federal Circuit chastised the district court for describing this hypothetical person as a pediatrician or general practitioner with experience in treating patients suffering from ear infections and a general knowledge of the pharmacology and use of antibiotics. Instead, the Federal Circuit focused on the inventors of the '741 patent themselves, stressing that they were "specialists in

drug and ear treatments," and that one was a university professor specializing in otorhinolaryngology, one was a research scientist engaged in the research and development of antibiotics, and the third was a Daiichi department manager engaged in the development and clinical trials of new drugs. App. 5a-6a. On this basis, the court of appeals ruled that

> the level of ordinary skill in the art of the '741 patent is that of a person engaged in developing pharmaceutical formulations and treatment methods for the ear or a specialist in ear treatments such as an otologist, otolaryngoloist, or otorhinolaryngologist who also has training in pharmaceutical formulations.

App. 6a.

Second, having thus described a substantially more expert person than someone having "ordinary" skill in the art, the court of appeals focused on a single piece of the prior art addressed by the district court. The court trained its attention on the 1986 Ganz article, which reported on the successful use of ear drops containing ciprofloxacin—not ofloxacin—to treat middle ear infections. App. 7a-9a. On this basis, the court held that a reasonable jury "would have no other choice" but to find that, in view of the Ganz reference, the use of ofloxacin in ear drops to topically treat ear infections would have been obvious to a person having ordinary skill in the art. App. 9a.

The court's exclusive emphasis on the Ganz article was remarkable for several reasons. Not only did the article concern a different antibiotic than the '741 patent, but, as the district court observed, the article actually taught away from the entire gyrase inhibitor family of antibiotics and stated that they should be

used only in difficult cases and only by the otologist. Apotex itself devoted only the most minimal attention to the article: a single sentence in Apotex's 62-page opening brief and nary a mention in the 30-page reply brief in the court of appeals. Moreover, although the parties filed a huge appendix in the court of appeals, full of trial exhibits, excerpts from the trial transcript, and other materials, Apotex chose not to include the testimony about the Ganz article that the court of appeals treated as so critical.

At the end of the day, the court of appeals simply substituted its judgment for that of the district court. Sitting in 2007 and reviewing a method patent that issued in 1995 for a specific use of an antibiotic patented in 1983, the court subjectively was not sufficiently impressed to sustain the patent. The court thus ignored the district court's findings regarding the Ganz article, and it also ignored the district court's findings about the long-felt medical need satisfied by the '741 patented invention and the commercial success of the FLOXIN® Otic product. At most, as the district court recognized, the prior art showed that it may have been "obvious to try" ofloxacin in an ear drop solution as a potential method for the topical treatment of bacterial ear infections. App. 42a. Under well-established law, however, what is "obvious to try" is not necessarily "obvious" for purposes of patent invalidity. *See, e.g.*, *In re Roemer*, 258 F.3d 1303, 1310 (Fed. Cir. 2001); *In re Eli Lilly & Co.*, 902 F.2d 943, 945 (Fed. Cir. 1990). The Federal Circuit's decision in this case obliterates this salutary distinction.

When the court of appeals issued its decision in July 2007, it designated its opinion as nonprecedential. On September 12, 2007, the day after the

court denied Daiichi's petition for rehearing, the court reissued its opinion as precedential, apparently at the behest of a law professor at the Northwestern School of Law of Lewis & Clark College, who wrote to the court and urged that the opinion be made precedential due to the importance of the court's ruling regarding the characteristics of the hypothetical person with "ordinary skill in the art."

REASONS FOR GRANTING THE PETITION

This Court in *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007), reversed the Federal Circuit, which previously had reversed a district court decision finding an invention obvious. The Court held that the Federal Circuit had applied too rigidly its so-called "teaching, suggestion, or motivation" test for determining whether a particular combination of prior art teachings would or would not have been obvious to a person having ordinary skill in the relevant art. This Court agreed with the district court that the prior art in *KSR* made obvious the combination of an electronic sensor with an adjustable automobile pedal using a fixed pivot point.

In the course of reaching this result, the Court remarked that under some circumstances "the fact that a combination was obvious to try might show that it was obvious under § 103." 127 S. Ct. at 1742. The present case, however, falls squarely outside that category, because, as the district court correctly found, Apotex failed to introduce clear and convincing evidence of prior art demonstrating that the new treatment method would have been a predictably safe and efficacious means of treating bacterial ear infections. The patented method, in other words, was

not predictably within the "technical grasp" of "a person of ordinary skill." *Id.*

The Federal Circuit's decision in the present case reflects a pendulum swing too far in the direction of holding patented inventions obvious. In the less than eight months since *KSR* was decided, the court of appeals has held inventions obvious in numerous cases. *See*, in addition to the present case, *Aventis Pharma. Deutschland GmbH v. Lupin, Ltd.*, 499 F.3d 1293 (Fed. Cir. 2007); *In re Translogic Tech., Inc.*, No. 2006-1192, 2007 WL 2965979, *1 (Fed. Cir. Oct. 12, 2007); *In re Icon Health and Fitness*, 496 F.3d 1374 (Fed. Cir. 2007); *In re Trans Texas Holdings Corp.*, 498 F.3d 1290 (Fed. Cir. 2007); *Leapfrog Enters., Inc. v. Fisher-Price, Inc.*, 485 F.3d 1157 (Fed. Cir. 2007); *Sygenta Seeds, Inc. v. Monsanto Co.*, 231 Fed. Appx. 954 (Fed. Cir. 2007).

Here, the court held the patented method obvious, even though an ofloxacin solution previously had not been demonstrated to be efficacious and safe for the topical treatment of bacterial ear infections and even though the patent issued only after the inventors undertook the extensive research needed to establish the unexpected result that such a topical solution could be used efficaciously without causing oto-toxicity or other systemic side effects. The court compounded the error by ignoring this Court's guidance that "[t]he question is not whether the combination was obvious to the patentee but whether the combination was obvious to any person of ordinary skill in the art." *KSR*, 127 S. Ct. at 1742. This Court should grant review to redress the imbalance of the court of appeals and to ensure that

inventions at most suggested for testing in the prior art are not for that reason deemed obvious.

I. "OBVIOUS TO TRY" DOES NOT EQUATE TO OBVIOUSNESS HERE, WHERE THE PATENTED DISCOVERY OF THE SAFETY AND EFFICACY OF THE TREATMENT METHOD RESULTED FROM THE INVENTORS' RESEARCH AND INNOVATION.

Although the court of appeals did not acknowledge the point, it is well settled that an accused infringer claiming obviousness must prove all relevant facts supporting the claim by clear and convincing evidence. *Polaroid Corp. v. Eastman Kodak Co.*, 789 F.2d 1556, 1558 (Fed. Cir. 1986); *Knoll Pharma. Co. v. Teva Pharmas. USA, Inc.*, 367 F.3d 1381, 1384 (Fed. Cir. 2004). The district court correctly found that Apotex did not carry that burden. In particular, the district court found that the Ganz article—the sole piece of prior art on which the court of appeals relied—did not render the '741 invention obvious. This was so for several reasons.

First, the Ganz article does not refer to the use of topical ofloxacin at all but only to another antibiotic in the gyrase inhibitor group, ciprofloxacin. Second, as the district court correctly observed, the Ganz article in a real sense teaches away from the '741 patent. Ganz declared that gyrase inhibitors such as ciprofloxacin were "antibiotics of second choice" for the treatment of ear infections and that such antibiotics should be used only in difficult cases and only by an otologist, not a general practitioner or pediatrician. Ganz thus stressed the safety concerns when using gyrase inhibitors, and safety was an

important aspect of the '741 method patent. A prior art reference that teaches away from, or discourages the practice of, the invention objectively supports the nonobviousness of the invention. *See, e.g., Bausch & Lomb, Inc. v. Barnes Hind/Hydrocurve, Inc.*, 796 F.2d 443, 448-49 (Fed. Cir. 1986), *cert. denied*, 484 U.S. 823 (1987). Third, although Ganz reported that no side effects were seen in the 20 patients treated with ciprofloxacin in the clinical study discussed in his article, he did not conclude that all gyrase inhibitors could be used for the topical treatment of bacterial ear infections without adverse effects. The court of appeals failed even to mention these factual findings by the district court, which could not have been overturned as clearly erroneous.

The court of appeals also disregarded the district court's factual findings and other evidence regarding mandatory, objective secondary considerations that tended to support nonobviousness. *See Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). The district court found, for example, that Daiichi's FLOXIN® Otic product was commercially successful, increasing its market share to 20 percent within the first five years of entering the market. The product's major competitor, a branded antibiotic called Cortisporin® Otic, suffered roughly a 30 percent loss of market share during the same period. In addition, the district court found that the '741 patent "satisfied a long felt medical need by providing physicians with a nonototoxic alternative to the available drugs to treat bacterial ear infections." App. 46a n.25. The court further explained that the invention "did not cause the same safety concerns of side effects, bacterial resistance, irritation of the middle ear mucosa and concentration of the drug absorbed in the blood stream, central nervous system and inner ear

perilymph as did conventionally available antibiotics." *Id.* The court of appeals did not disturb any of these factual findings; it just disregarded them. In addition, although not cited by the district court or acknowledged by the court of appeals, Daiichi introduced extensive, uncontroverted evidence of unexpected results and significant industry recognition attributable to the '741 patented treatment method. A6158-62; A9699-9732; A11285-86; A11302-05; A11312-17; A11515-16; A11525-30.

Perhaps most significantly, and most indicative of an unjustified shift in the court of appeals' approach to the obviousness inquiry, the court eliminated, or at least substantially blurred, the longstanding distinction between prior art that merely suggests trying a research or development program but without suggesting the particular method or expected results, and prior art that renders an invention obvious. A prior art reference that invites one of ordinary skill in the art to experiment or explore, but does not contain a specific teaching of how to obtain the invention or that the invention would be obtained if certain tests were performed, does not render the invention obvious. *In re Eli Lilly & Co.*, 902 F.2d at 945. Here, the prior art at most suggested that ofloxacin might be tried in an ear drop solution. It did not disclose what would happen if that research were conducted, whether the solution would be sufficiently efficacious in treating bacterial ear infections, and whether such a solution could be administered topically into the ear without ototoxicity or other systemic safety concerns. The utility and safety of the invention were determined only through the research and innovation of the inventors. Their results and their invention were neither predictable nor obvious to one of ordinary skill.

II. THE COURT OF APPEALS FURTHER ERRED IN ITS OBVIOUSNESS INQUIRY BY USING THE INVENTORS' OWN EDUCATION, EXPERIENCE, AND SKILL AS A BASIS FOR DETERMINING THE CHARACTERISTICS OF A HYPOTHETICAL PERSON WITH ORDINARY SKILL IN THE ART.

By relying on the education, experience, and skill level of the inventors as a basis for determining the characteristics of the hypothetical person with ordinary skill in the art, the Federal Circuit compounded its error. Judge Rich explained why in a leading opinion for the Federal Circuit more than 20 years ago. *Standard Oil Co. v. American Cyanimid Co.*, 774 F.2d 448, 454 (1985). Put simply, an inventor cannot be the standard against which his own inventiveness is measured. Otherwise, the inventor would be penalized for his own superior skill, learning, and experience. In Judge Rich's memorable words,

> The actual inventor's skill is irrelevant to the inquiry, and this is for a very important reason. The statutory emphasis is on a person of *ordinary* skill. Inventors, as a class, according to the concepts underlying the Constitution and the statutes that have created the patent system, possess something-call it what you will-which sets them apart from the workers of *ordinary* skill, and one should not go about determining obviousness under § 103 by inquiring into what *patentees* (i.e., inventors) would have known or would likely have done, faced with the revelations of references. A person of ordinary skill in the art is also presumed to be one who thinks along the line of conventional wisdom in

> the art and is not one who undertakes to innovate, whether by patient, and often expensive, systematic research or by extraordinary insights, it makes no difference which.

A recent commentator has made essentially the same point. "[T]he test does not ask what would have been subjectively obvious to the inventor. Instead the court must determine whether the invention would have been objectively obvious to the hypothetical person having ordinary skill in the art at the time the invention was made. Without evaluation from the perspective of one of ordinary skill in the art, most inventions would be deemed obvious because the decision-maker could merely piece together elements from the prior art using the invention as a blueprint." Joseph P. Meara, *Just Who Is The Person Having Ordinary Skill in the Art? Patent Law's Mysterious Personage*, 77 Wash. L. Rev. 267, 276-77 (2002) (footnotes omitted).

The Federal Circuit in this case departed from this prudent standard. It looked to the inventors of the '741 patent as if their knowledge, learning, and experience would be determinative of that of the person with ordinary skill in the art. On that basis, the court focused its attention on a narrow and highly trained group of experts comprising only a comparatively small number of people. Working backward from the '741 invention, the court then declared that others in the expert group could have concluded from the prior art that the use of an ofloxacin solution for the topical treatment of bacterial ear infections would have been both efficacious and safe.

This mode of analysis is firmly grounded in impermissible hindsight. It starts with the invention

and its proven success and then looks at the prior art and speculates about whether some other persons as competent as the inventors might have conducted the same research as the inventors and eventually reached the same findings and conclusions. As the district court correctly recognized, that is not the way the obviousness inquiry is supposed to be conducted. The inventors' own expertise and research work cannot be used against them to determine what others might have done, in the absence of any evidence suggesting the research method and results achieved by the inventors.

Finally, on at least three separate occasions in its opinion, the court of appeals refers to the creation or development of a "compound" as the art involved in the '741 patent. App. 5a, 6a (twice). But that is not an accurate characterization of the '741 patent's claimed method of treatment. It is undisputed that at the time of the invention the compound ofloxacin was known. It had been patented several years earlier. It did not need to be created or developed. What did need to be created and developed was a *method* for using ofloxacin as a topical ear infection treatment that was both efficacious and safe. That is what the inventors did through an extensive research effort, the method and results of which are laid out in the '741 patent for the first time. Daiichi eventually brought to the market a new treatment method that was recognized as a breakthrough in the safe and efficacious treatment of bacterial ear infections. App. 19a. Review in this Court is needed to rectify the Federal Circuit's overbroad view of obviousness and to confirm the correctness of the district court's judgment based on that court's detailed and well-supported findings of fact.

CONCLUSION

The petition for a writ of certiorari should be granted.

Respectfully submitted,

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December 10, 2007

APPENDIX

APPENDIX A

United States Court of Appeals
for the Federal Circuit

2006-1564

DAIICHI SANKYO CO., LTD. (formerly known as DAIICHI PHARMACEUTICAL CO., LTD.) and DAIICHI SANKYO, INC. (formerly known as DAIICHI PHARMACEUTICAL CORPORATION),
Plaintiffs-Appellees,

v.

APOTEX, INC. and APOTEX CORP.,
Defendants-Appellants.

Brian P. Murphy, Morgan, Lewis & Bockius LLP, of New York, New York, argued for plaintiffs-appellees. With him on the brief were *David Leichtman, Daniel Murphy*, and *Oren D. Langer*. Of counsel on the brief was *James P. Flynn*, Epstein, Becker & Green, PC, of Newark, New Jersey.

Robert B. Breisblatt, Welsh & Katz, Ltd., of Chicago, Illinois, argued for defendants-appellants. With him on the brief were *A. Sidney Katz, Julie A. Katz, Philip D. Segrest, Jr.*, and *Michael A. Krol*. Of counsel on the brief was *Steven Gerber*, Adorno & Yoss, LLP, of Wayne, New Jersey.

Appealed from: United States District Court for the District of New Jersey

Senior Judge William G. Bassler

United States Court of Appeals
for the Federal Circuit

2006-1564

DAIICHI SANKYO CO., LTD. (formerly known as DAIICHI PHARMACEUTICAL CO., LTD.) and DAIICHI SANKYO, INC. (formerly known as DAIICHI PHARMACEUTICAL CORPORATION),
Plaintiffs-Appellees,

v.

APOTEX, INC. and APOTEX CORP.,
Defendants-Appellants.

DECIDED: July 11, 2007

Before MICHEL, *Chief Judge*, ARCHER, *Senior Circuit Judge*, and DYK, *Circuit Judge*. ARCHER, *Senior Circuit Judge*.

Apotex, Inc. and Apotex Corp. (collectively "Apotex") appeal the judgment of the United States District Court for the District of New Jersey that Apotex infringes U.S. Pat. No. 5,401,741 ("the '741 patent") and that the '741 patent is not invalid or unenforceable. *Daiichi Pharm. Co. v. Apotex, Inc.*, 441 F. Supp. 2d 672 (D.N.J. 2006) ("*Validity Determination*"). Because the invention of the '741 patent would have been obvious in view of the prior art, we *reverse*.

The '741 patent is drawn to a method for treating bacterial ear infections by topically administering the

antibiotic ofloxacin into the ear.[1] Claim 1 is representative and states "[a] method for treating otopathy which comprises the topical otic administration of an amount of ofloxacin or a salt thereof effective to treat otopathy in a pharmaceutically acceptable carrier to the area affected with otopathy." '741 Patent, col.6 ll.36-39.

Apotex filed an Abbreviated New Drug Application ("ANDA") seeking approval to manufacture a generic ofloxacin ear drop, including a ¶ IV certification that the '741 patent was invalid and/or not infringed. Following receipt of the ANDA, Daiichi, owner of the '741 patent, sued Apotex for infringement. Following a *Markman* hearing, the district court construed the claim term "effective to treat" as "efficacious and safe." Based on this construction and following a bench trial, the court concluded that the '741 patent was not invalid. The court also found that Daiichi did not intend to deceive the Patent and Trademark Office during prosecution of the '741 patent. Finally, because Apotex stipulated that the subject matter of its ANDA fell within the scope of the claims of the '741 patent, the court found that Apotex infringed the '741 patent.

Apotex appeals, and we have jurisdiction pursuant to 28 U.S.C. 1295(a)(1).

II

Obviousness is a question of law based on underlying questions of fact. *Winner Int'l Royalty Corp. v. Wang*, 202 F.3d 1340, 1348 (Fed. Cir. 2000). Thus, we review the ultimate determination of obviousness by a district court *de novo* and the underlying factual inquiries for clear error. *Id.*

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[1] The '741 patent has an effective filing date of April 8, 1988.

The underlying factual inquiries in an obviousness analysis include: "(1) the scope and content of the prior art; (2) the level of ordinary skill in the prior art; (3) the differences between the claimed invention and the prior art; and (4) objective evidence of nonobviousness." *In re Dembiczak*, 175 F.3d 994, 998 (Fed. Cir. 1999). In this case, we begin our analysis with the question of the level of ordinary skill in the prior art.

The district court concluded that the ordinary person skilled in the art pertaining to the '741 patent "would have a medical degree, experience treating patients with ear infections, and knowledge of the pharmacology and use of antibiotics. This person would be . . . a pediatrician or general practitioner—those doctors who are often the `first line of defense' in treating ear infections and who, by virtue of their medical training, possess basic pharmacological knowledge." *Daiichi Pharm. Co. v. Apotex, Inc.*, 380 F. Supp. 2d 478, 485 (D.N.J. 2005) ("*Claim Construction Order*"). Apotex argues that the district court clearly erred in this determination and that one having ordinary skill in the relevant art is properly defined as "a person engaged in developing new pharmaceuticals, formulations and treatment methods, or a specialist in ear treatments such as an otologist, otolaryngologist, or otorhinolaryngologist who also has training in pharmaceutical formulations."

"Factors that may be considered in determining level of ordinary skill in the art include: (1) the educational level of the inventor; (2) type of problems encountered in the art; (3) prior art solutions to those problems; (4) rapidity with which innovations are made; (5) sophistication of the technology; and (6) educational level of active workers in the field." *Envtl.*

Designs, Ltd. v. Union Oil Co., 713 F.2d 693, 696 (Fed. Cir. 1983) (citing *Orthopedic Equip. Co., Inc. v. All Orthopedic Appliances, Inc.*, 707 F.3d 1376, 1381-82 (Fed. Cir. 1983)). These factors are not exhaustive but are merely a guide to determining the level of ordinary skill in the art.

In making its determination regarding the level of skill in the art, the district court noted that the parties had provided "little more than conclusory arguments concerning this issue in their briefs." As a result, the court looked to other decisions involving patents for a method of treating a physical condition for guidance. Only one case cited by the district court is binding on us, *Merck & Co., Inc. v. Teva Pharm. USA, Inc.*, 347 F.3d 1367 (Fed. Cir. 2003). The district court was correct that in that case we affirmed the trial court's conclusion that a person having ordinary skill in the relevant art was a person having a medical degree, experience treating patients with osteoporosis, and knowledge of the pharmacology and usage of biphosponates—the compounds at issue in *Merck*. However, in *Merck* the level of skill in the art was not disputed by the parties. Thus, we simply accepted the district court's finding. That clearly is not the case before us. Therefore, the district court's reliance on the level of skill in the art stated in *Merck* was improper.

The art involved in the '741 patent is the creation of a compound to treat ear infections without damaging a patient's hearing. The inventors of the '741 patent were specialists in drug and ear treatments—not general practitioners or pediatricians. At the time of the invention, Inventor Sato was a university professor specializing in otorhinolaryngology; Inventor Handa was a clinical development department manager

at Daiichi, where he was involved with new drug development and clinical trials; and Inventor Kitahara was a research scientist at Daiichi engaged in the research and development of antibiotics. Additionally, others working in the same field as the inventors of the '741 patent were of the same skill level. *See* Daiichi *Material for [C]onference on Development*, Nov. 11, 1987 (stating that "there are many voices among medical persons concerned with otorhinolaryngology for demanding development of an otic solution making use of [ofloxacin]").

Further, the problem the invention of the '741 patent was trying to solve was to create a topical antibiotic compound to treat ear infections (otopathy) that did not have damage to the ear as a side effect. '741 Patent, col.1 ll.23-34. Indeed, most of the written description details the inventors' testing ofloxacin on guinea pigs and their findings that ototoxicity did not result from the use of their compound. Such animal testing is traditionally outside the realm of a general practitioner or pediatrician. Finally, while a general practitioner or pediatrician could (and would) prescribe the invention of the '741 patent to treat ear infections, he would not have the training or knowledge to develop the claimed compound absent some specialty training such as that possessed by the '741 patent's inventors. Accordingly, the level of ordinary skill in the art of the '741 patent is that of a person engaged in developing pharmaceutical formulations and treatment methods for the ear or a specialist in ear treatments such as an otologist, otolaryngologist, or otorhinolaryngologist who also has training in pharmaceutical formulations. Thus, the district court clearly erred in finding otherwise.

We now turn to the question of whether the invention of the '741 patent would have been obvious to one of ordinary skill in the art at the time of the invention. The district court's error in determining the level of ordinary skill in the art of the '741 patent tainted its obviousness analysis. In view of the correct level of skill in the art and the evidence of record, we conclude that as a matter of law the '741 patent is invalid as obvious.

The district court construed "effective to treat" to include not only efficacy but safety. We need not decide whether safety is a positive limitation, because the evidence demonstrates that in view of the correct level of skill in the art using a topical formulation of ofloxacin to treat ear infections was not only obvious but safe.

An article published in 1986, taught the successful use of ear drops containing ciprofloxacin to treat middle ear infections. *Gyrase inhibitor in local treatment of middle ear radical cavities chronically infected with problem microorganisms*, HNO vol. 34, 511 (1986) (teaching a lack of ototoxicity for ciprofloxacin administered topically) ("*Ganz*"). This article explained that ciprofloxacin "would definitely have to be suitable for use as eardops" because ciprofloxacin, a gyrase inhibitor, was not subject to the drawbacks normally associated with local treatment of the ear with antibiotics, such as ototoxicity. *Id.* The subjects' ear infections were treated locally with a ciprofloxacin solution, and "[i]n not one case were side effects of any kind observed." *Id.* at 512.

The district court dismissed this finding of no side effects, and thus no ototoxicity, because the article reported that use of gyrase inhibitors "should be used only in difficult cases and exclusively by the otologist."

Because an otologist was outside the level of ordinary skill in the art as determined by the district court, the district court found that the reference did not support Apotex's argument that ofloxacin, a gyrase inhibitor like ciprofloxacin, was effective and safe to treat bacterial ear infections topically.[2] As explained above, the district court's determination of the level of ordinary skill in the art was incorrect; thus, so, too, was its dismissal of the teaching of the *Ganz* reference.

When testifying as to the relevance of the *Ganz* reference in 1988, Apotex's expert explained that ciprofloxacin is an antibiotic that is in the same family as ofloxacin, and thus "[o]ne would understand that a very close relative to Ciprofloxacin [sic] was safe and effective in treatment of middle ear disease, otitis media." Trial Tr. Vol. 3, 73-74 Nov. 3, 2005. When asked specifically what the *Ganz* reference would teach to one of ordinary skill in the art with regard to ofloxacin, he further opined that "someone of ordinary skill in the art would be taught that Ofloxacin [sic] would be very likely equally as effective as Ciprofloxacin [sic] when used topically to treat middle ear infections" and "one would also think it would be highly likely that Ofloxacin [sic] could be used in the middle ear with safety." *Id.* at 77. This testimony was based on the *Ganz* reference's statement that no side effects were observed combined with the fact that ofloxacin and ciprofloxacin were both from the same drug family (gyrase inhibitors). *Id.* at 77, 61. This testimony was not disputed by Daiichi's expert except on the basis that the *Ganz* reference did not convey

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[2] Presumably, this explains why the district court did not refer to ofloxacin's similarity to ciprofloxacin in its opinion.

the same teaching to one of lower skill in the art such as a practicing physician.

Daiichi's expert opined that the *Ganz* reference disclosed "nothing at all" relevant. This opinion was based on the fact that the article was directed at "a highly, highly subspecialized physician . . . which would be the otologist or the ear doctor" not a primary care physician or general practitioner. Trial Tr. Vol. 7, 72-73 Nov. 11, 2005. He further explained that the article did not render the invention of the '741 patent obvious "most importantly because those of ordinary skill are defined as a population ... of physicians that are completely different than the audience Dr. Ganz [the author] was writing to." *Id.* at 73-74. Thus, Daiichi's evidence as to why this reference did not render the invention of the '741 patent obvious was based on an improper determination of the level of skill in the art.[3]

Accordingly, the evidence demonstrates that a reasonable jury would have no other choice than to conclude that, in view of the *Ganz* reference, it would have been obvious to a person engaged in developing pharmaceutical formulations and treatment methods for the ear or to a specialist in ear treatments who also has training in pharmaceutical formulations to use ofloxacin in ear drops to topically treat ear infections.[4]

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[3] Daiichi's only evidence with respect to this reference that does not rely on the level of skill in the art is its expert's conclusory statement that "[o]ne cannot extrapolate a safety profile for one antibiotic to another." This unsupported statement cannot refute the detailed testimony of Apotex's expert.

[4] Claim 4 of the '741 patent recites a concentration range for the ofloxacin in the compound—"about 0.05 to about 2% w/v."

III

Because the invention of the '741 patent would have been obvious to one having ordinary skill in the art at the time of the invention, the judgment of the district court[5] is reversed.

One of the prior art references, U.S. Patent No. 4,551,456, teaches the use of ofloxacin in antibiotic compounds where ofloxacin makes up "0.03 to 3% and especially 0.15% to 0.5%" of the compound. Col.1 ll. 37-39. Thus, the range claimed in the '741 patent falls within the scope of the prior art.

[5] Because we hold the '741 patent invalid as obvious, we need not reach Apotex's arguments that the '741 patent was anticipated or procured through inequitable conduct.

APPENDIX B

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

Civ. No. 03-937 (WGB)

DAIICHI PHARMACEUTICAL CO., LTD. and DAIICHI PHARMACEUTICAL CORPORATION,
Plaintiffs,

v.

APOTEX, INC. and APOTEX CORP.,
Defendants.

OPINION

APPEARANCES:

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BASSLER, SENIOR DISTRICT JUDGE:

In this patent infringement action,[1] Plaintiffs, Daiichi Pharmaceutical Co. Ltd., a Japanese drug manufacturer, and its New Jersey-based subsidiary, Daiichi Pharmaceutical Corporation (collectively, "Daiichi") sued Apotex Inc., a Canadian-based generic drug manufacturer, and its subsidiary, Apotex Corp. (collectively, "Apotex"). Daiichi claims that Apotex infringed on Daiichi's Patent No. 5,401,741 ("'741 patent").

The First Amended Complaint alleges willful patent infringement under the Hatch-Waxman Act, 35 U.S.C. § 271(e)(2), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202, and 35 U.S.C. § 271(a), (b) and/or (c).[2] Apotex denies Daiichi's allegations and raises the following defenses: (1) patent invalidity; (2) anticipation; (3) obviousness; (4) unenforceability; (5)

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[1] This matter was tried without a jury before this Court on November 1-3, 8-10 and 15-17. Jurisdiction and venue in this district are proper pursuant to 28 U.S.C. §§ 1331, 1338(a), 1391(b) and 1400(b).

[2] In a stipulation dated October 5, 2005, Daiichi agreed, among other things, to dismiss, without prejudice, its second cause of action for a declaratory judgment of patent infringement and for an injunction pursuant to 35 U.S.C. § 283, as pleaded in Daiichi's First Amended Complaint for patent infringement dated May 26, 2004.

noninfringement; (6) noninfringement of claim 7; and (7) misuse. Apotex filed a counterclaim against Daiichi.[3] Magistrate Judge Arleo severed Counts 7-11 of the counterclaim, which were not directly related to the infringement action and stayed proceedings regarding the severed counts pending trial on the issue of infringement. *See* September 1, 2004 Discovery and Case Management Order.

For the reasons set forth below, the Court finds that the '741 patent is not invalid or unenforceable. Furthermore, the Court determines that Apotex infringed on Daiichi's '741 patent.

I. FINDINGS OF FACT

These findings of fact constitute the Court's final determination of contested factual issues and therefore supersede any prior recitation of facts contained in Opinions previously entered on the docket. The Court makes these findings of fact pursuant to Fed. R. Civ. P. 52. Before the Court sets forth its findings, it wishes to elaborate on the procedure it utilized to arrive at its factual determinations.

The Court invited the parties to submit proposed findings of fact and conclusions of law, and responses thereto, after the close of testimony.[4] The final pro-

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[3] The 11 Counts of Apotex's counterclaim are: Count 1- Declaration of Invalidity, Count 2-Declaration of Anticipation, Count-Declaration of Obviousness, Count 4-Declaration of Unenforceability, Count 5-Declaration of Infringement, Count 6-Declaration of Non-Infringement of Claim 7, Count 7- Monopolization in Violation of the Sherman Act § 2, Count 8- Attempt to Monopolize in Violation of the Sherman Act § 2, Count 9-Unreasonable Restraint of Trade in Violation of Sherman Act § 1, Count 10-Declaration of Patent Misuse and Count 11-Tortious Interference with a Prospective Business Relation.

[4] Citations to Plaintiffs' Proposed Findings of Fact or Pro-

posed finding of fact submission was filed February 17, 2006. The Court has carefully reviewed the proposed findings, the documentary evidence and the testimony adduced at trial. The Court, having considered this array of information, sets forth its findings of fact based on its independent review of the evidence and utilizes the parties' proposed findings of fact merely to assist the Court in organizing this information. *See* 9A Wright & Miller, Federal Practice and Procedure: Civil 2d § 2578 (1995) ("Proposed findings submitted by counsel are no more than informal suggestions for the sole purpose of assisting the court.")

The Court bases its findings of fact on its careful consideration of the testimony adduced at trial and a review of the documentary evidence submitted, as well as the logical inferences to be drawn from them. In evaluating the evidence of record, the Court undertook an individualized assessment of the credibility of each witness and assigned the appropriate weight to the testimony based on the Court's conclusions with respect to credibility.[5]

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posed Conclusions of Law and Defendants' Proposed Findings of Fact or Proposed Conclusions of Law will be cited to as PPFF, PPCL, DPFF and DPCL respectively. Furthermore, citations to the trial transcript ("Trial Tr.") include the name of the witness who was testifying, volume number and page number. Citations to trial exhibits are to Plaintiff's Trial Exhibits ("PTX") and to Defendants' Trial Exhibits ("DTX").

[5] In assessing the credibility of each witness in this case, the Court has taken into consideration how well each witness was able to recall and describe the things testified to, the manner of the witness while testifying, whether the witness had an interest in the outcome of the case or any bias or prejudice concerning any party or matter involved in the case, whether the witness' testimony was contradicted by what that witness

To the extent that any of the findings of fact might constitute conclusions of law, they are adopted as legal conclusions. Conversely, to the extent that any conclusions of law constitute findings of fact, they are adopted as factual determinations.

A. The Parties

Daiichi Pharmaceutical Co., Ltd. ("DSK") is a Japanese corporation having its principal place of business in Tokyo, Japan. (Trial Tr. Vol. 2, 101:21-24). DSK is the owner of all right, title and interest in the '741 patent, entitled "Topical Preparation for Treating Otopathy," issued on March 28, 1995. The patent was issued in the name of inventors Kiichi Sato, Akira Handa and Takeji Kitahara—all of Japan, who assigned their right to the patent to DSK. (PTX 1 at 2; PTX 4; PTX 5 at 2, patent application number 622, 121; Trial Tr. Vol. 2, 102:8-15; Defendants' Answer to First Amended Complaint dated June 23, 2004 at ¶ 7). DSK is also the holder of New Drug Application ("NDA") No. 20-799 for FLOXIN® Otic (Ofloxacin Otic Solution, 0.3%), which was approved by the U.S. Food and Drug Administration ("FDA") on December 16, 1997. (PTX 31 at DPC-04 00007; PTX 32 at DPC-03 01363; Defendants' Answer to First Amended Complaint dated June 23, 2004 at¶ 9).

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had said or done at another time, by the testimony of other witnesses, or by other evidence and how reasonable the witness' testimony was in light of all the evidence in the case. *Miller v. Mercy Hospital, Inc.*, 720 F.2d 356, 365 (4th Cir. 1983), *cert. denied*, 470 U.S. 1083 (1985) (citing 9A Wright & Miller, Federal Practice and Procedure: Civil 2d § 2586 (1995))("Credibility involves more than a witness' demeanor and comprehends an overall evaluation of testimony in light of its rationality or internal consistency and the manner in which it hangs together with other evidence.").

Daiichi Pharmaceutical Corporation ("DPC") is a Delaware corporation with its principal place of business in Montvale, New Jersey and a wholly owned subsidiary of DSK. (Trial Tr. Vol. 2, 101:25-102:4). DPC is the sales and marketing arm of DSK in the United States (Trial Tr. Kane, Vol. 8, 31:9-13). DPC has been and remains the agent of DSK for the filing and regulatory review of NDA No. 20-799 and has an exclusive license to market and sell FLOXIN® Otic in the United States and Puerto Rico (PTX 31 at DPC04 00007; PTX 32 at DPC-03 01363; Trial Tr. Kane, Vol. 8, 45:23-46:3).

The approved treatment indications for FLOXIN® Otic medicine are i) Otitis Externa in adults and pediatric patients, one year and older; ii) Acute Otitis Media in pediatric patients one year and older with tympanostomy tubes; and (iii) Chronic Suppurative Otitis Media in patients 12 years and older with perforated tympanic membranes, caused by the designated microorganims. (PTX 7C at 2, "Indications and Usage"; PTX 31 at DPC-03 10426. PTX 47 at A000087; PTX 78 at 3, "Indications and Usage").

Apotex, Inc. is a privately held Canadian corporation having its principal place of business in Weston, Ontario, Canada. (Trial Tr. Vol. 2 102:5-7). On or about October, 25, 2002, through its Novex Pharma division, Apotex filed Abbreviated New Drug Application ("ANDA") No.76-527 with the U.S. Food and Drug Administration ("FDA") requesting approval to market and sell a generic version of Daiichi's FLOXIN® Otic in the United States for the same FDA-approved treatment indications as FLOXIN® Otic. (PTX 47 at A00001 and 000057; Defendants' Answer to First Amended Complaint dated June 23, 2004 at ¶ 10). Daiichi was given notice by letter of Apotex's ANDA submission

pursuant to Section 505(j)(2)(B)(ii) of the Federal Food, Drug and Cosmetic Act (21 CFR § 314.95(c)) requesting marketing approval to manufacture, use or sell Ofloxacin Otic Solution, 0.3% prior to the expiration of the '741 patent. (Defendants' Answer to First Amended Complaint dated June 23, 2004 at ¶ 11). Apotex Corp. has been designated by Apotex, Inc. to act as Apotex Inc.'s sole agent in the U.S. in all matters relating to the ANDA. (PTX 47 at A000057; Trial Tr. Vol. 2, 103:6-12). Apotex's ANDA included a "Paragraph IV Certification," challenging the validity and infringement of Daiichi's '741 patent. (PTX 47 at A000068).[6]

B. '741 Patent

The '741 patent is directed to a method for treating bacterial ear infections by topically administering the antibiotic known as ofloxacin into the ear (PTX 1 at Col. 1, lines 58-64, Col. 5, lines 49-50; *Daiichi Pharm. Co., v. Apotex, Inc.*, 380 F. Supp. 2d 478, 481, 488-89 (D.N.J. 2005)).[7] Ofloxacin is the only antimicrobial

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[6] Since the close of trial, Apotex's ANDA has been reviewed and approved by the FDA on November 18, 2005.

[7] The 741 patent sets forth seven claims:

> Claim 1: A method for treating otopathy which comprises the topical otic administration of an amount of ofloxacin or a salt thereof effective to treat otopathy in a pharmaceutically acceptable carrier to the area affected with otopathy.
>
> Claim 2: The method of claim 1 wherein the said otopathy is otitis media.
>
> Claim 3: The method of claim 2 wherein the said otopathy is otitis externa.
>
> Claim 4: The method of claim 2 wherein the concentration of ofloxacin in the pharmaceutically acceptable carrier is about 0.05 to about 2t w/v.

compound in Daiichi's eardrops; it has no other active ingredients. (Trial Tr. Klein, Vol. 2, 54:13-24).[8] Daiichi's patented method of treatment covers the

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> Claim 5: The method as claimed in claim 4, wherein the dosage form of ofloxacin is an aqueous solution.
>
> Claim 6: The method as claimed in claim 5, wherein the aqueous solution of ofloxacin is applied to the external auditory canal by instillation.
>
> Claim 7: The method as claimed in claim 6, wherein the aqueous solution of ofloxacin is intratympanically injected through a puncture in the tympanic membrane.

After holding a Markman hearing on July 22, 2005, the Court held that a person ordinarily skilled in the art would have a medical degree, experience treating patients with ear infections, and knowledge of the pharmacology and use of antibiotics. *Daiichi Pharm. Co.*, 380 F. Supp. 2d at 485. Additionally, that person would be a pediatrician or general practitioner-those doctors who are often the first line of defense in treating ear infections. *Id.* Furthermore, the Court construed the term "otopathy" to mean "bacterial ear infection," the words "effective to treat" to be interpreted as "safe and efficacious," and the phrase "intratympanically injected through a puncture of the tympanic membrane" to mean "introduced into the middle ear with an instrument such as a syringe." *Id.* at 485-89. Consequently, the parties stipulated that the method for which Apotex seeks approval in its ANDA No. 76-527, "is not within the scope of, or covered by, the literal language of claim 7 of the '741 patent, or an equivalent thereof, as it has been construed by the Court" in the Markman Hearing. (PTX 313 ¶ 4). Subsequently, the parties stipulated that Daiichi would withdraw with prejudice its claim that Apotex's ANDA No. 76-527 infringes Claim 3 of the '741 patent. *See* March 28, 2006 Stipulation.

[8] Daiichi obtained a patent on the compound of ofloxacin, U.S. patent 4,382,892 ("Hayakawa '892"). (DTX 40; DTX 17 at D0055-64, 70, 71). Daiichi submitted this patent in its application of the '741 patent and acknowledged that it was the assignee of both the '741 and '892 patents. (DTX 17 at D0071). The '892 patent expired on September 2, 2001. 35 U.S.C. § 154(a)(2).

use of its FLOXIN® Otic product. (PTX 7C; PTX 78).[9] The '741 patent claims priority from Japanese Patent Application No. 86378/88, filed in Japan on April 8, 1988. (PTX 1 at 2, left column; PTX 6; PTX 6A; Trial Tr., Vol. 2, 102:16-18).[10]

The '741 patent discloses and claims that the topical otic administration of ofloxacin is safe and efficacious to treat bacterial ear infections (PTX 1 at Col. 2, line 30—Col. 6, line 55; Trial Tr. Klein, Vol. 2, 35:13-25; Trial Tr. Dohar, Vol. 7, 27:12-16; *Daiichi Pharm. Co.*, 380 F. Supp. 2d at 488). FLOXIN® Otic was the first antibiotic ear drop medicine ever approved by the FDA for treating bacterial ear infections in pediatric and adult patients who have a perforation in their ear drum. (PTX 185 at DSK-06 09300; Trial Tr. Dohar, Vol. 7, 15:1-9; *Daiichi Pharm. Co.*, 380 F. Supp. 2d at 482). Prior to the time of the '741 patent, the available ototopical (ear drop) drugs were known to be ototoxic—i.e., they had a propensity to cause (i)

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[9] As its title indicates, the '741 patent is a "method" patent, as compared to a machine, composition, or manufacture patent. One treatise explains: "the 'elements' of a method claim, instead of being structural parts, are, and must be, acts or manipulative steps that are performed upon an article, workpiece, or chemical substance. It is the transformation or reduction of the article, workpiece, or chemical substance to a different state or thing that is the essence of a method claim - and the key to its patentability." Robert C. Faber, Landis on Mechanics of Patent Claim Drafting § 4:1(5th ed. 2004).

[10] This date is critical to Apotex's invalidity argument because prior art that disclosed the elements of the '741 patent claims may anticipate or make obvious the patent, which would invalidate it. Prior art is defined as "that reasonably pertinent to the particular problem which the inventor was involved." *Hilton Davis Chemical Co. v. Warner-Jenkinson Co.*, 62 F.3d 1512 (Fed. Cir. 1995), *rev'd on other grounds* , 520 U.S. 17 (1997).

hearing impairment, by damaging the cochlea and its hair cells, and/or (ii) balance impairment, by damaging the vestibular system. (Trial Tr. Klein, Vol. 1, 114:8-24; Trial Tr. Hain, Vol. 3, 119:6-120:8; *Daiichi Pharm. Co.*, 380 F. Supp. 2d at 481-82).

The risk of ototoxicity can occur when an antibiotic compound is applied directly to the middle ear or where the tympanic membrane has been ruptured. (Trial Tr. Klein, Vol. 1, 115:1-25).[11] There are, therefore, at least two situations that present the risk of ototoxicity. First is when a patient suffers from otitis media, a bacterial infection of the middle ear. Second is when a patient suffers from otitis externa, a bacterial infection of the external auditory canal, with a ruptured tympanic membrane.[12] The risk of ototoxicity was present when using ear drops to treat otitis externa because there could be a perforation of the ear drum not appreciated by the physician. (PTX 153 at DSK-06 09694-95—*see* "Cortisporin® Otic Solution"—"Precautions"; PTX 314 at 7 ("Otitis externa is easily diagnosed by looking into the external ear with an otoscope. The main problem with diagnosis is deciding whether or not there is also an otitis media, as often

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[11] To understand these risks, it is helpful to know that the ear consists of three chambers: (1) the outer ear, including the external auditory canal, which focuses sound waves on the tympanic membrane (commonly known as the ear drum); (2) the middle ear, which conducts sound; and (3) the inner ear, which transmits sound vibrations to the auditory nerve for processing into sound. (Trial Tr. Klein, Vol. 1, 89:19-93:23). The tympanic membrane separates the external auditory canal from the middle ear. (Trial Tr. Klein, Vol. 1, 90:17-91:8).

[12] Otitis media and otitis externa are characterized by localized pain, swelling, and inflammation. Otitis externa is commonly referred to as "swimmer's ear." (Trial Tr. Klein, Vol. 1, 99:4-13; 109:18-20; 114:6-7).

one cannot see the ear drum very well as the external ear canal is swollen, painful and filled with debris.")). Therefore, physicians were warned to act with care when the integrity of the ear drum was in question. (Trial Tr. Klein, Vol. 1, 115:10-12).

Prior to the time of the '741 patent, none of the available ototopical eardrop preparations were free from the ototoxic safety concern. (Trial Tr. Dohar, Vol. 7, 11:22-12:6; Trial Tr. Hain, ,Vol. 3, 55:9-57:5; DTX 47 at A006983). All of the otic formulations for ear drops listed in the Physicians Desk Reference ("PDR") carried contraindications to their use in the face of a nonintact ear drum. (Trial Tr. Dohar, Vol. 7, 15:1-9; PTX 153 at DSK-06 09694-95 - *see* "Cortisporine Otic Solution" - "Precautions"; PTX 315 at 1532 - *see* "Chloromycetin® Otic" - "Precautions").

Use of systemic antibiotics (absorbed into the bloodstream) also raised the concern of the development of bacterial resistance and other side effects such as diarrhea, vomiting and allergic reactions. (Trial Tr. Klein, Vol. 1, 112:4-113:11; *Daiichi Pharm. Co.,* 380 F. Supp. 2d at 481). Use of systemic antibiotics such as gentamicin and neomycin also were known to cause ototoxic side effects. (Trial Tr. Hain, Vol. 3, 120:9-121:16-122:4; 124:14-24).

In addition, there were no FDA-approved oral antibiotics for use in children to treat ear infections caused by pseudomonas aeruginosa prior to the '741 patent. (Trial Tr. Dohar Vol. 7, 12:7-13:4). Pseudomonas aeruginosa is one of the primary pathogens that causes ear infections. (PTX 21, 99:9-22; Trial Tr. Klein, Vol. 1, 107:23-108:7; Trial Tr. Dohar, Vol. 7 12:21- 13:4).[13] Prior to April 8, 1988,

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[13] Ofloxacin also is effective against other bacteria, including

pseudomonas aeruginosa was known to be resistant to amoxicillin[14] and neomycin, which were used to treat bacterial ear infections. (Trial Tr. Dohar Vol. 3, 117:18-24).

The method described in the '741 patent was intended to overcome these risks, by setting forth a method for the topical administration of ofloxacin—a previously known antibiotic compound—to both the external auditory canal and the middle ear, while significantly reducing the risk of ototoxicity and antibacterial resistance. (Trial Tr. Klein, Vol. 2, 13:12-13, 35:19-25; *Daiichi Pharm. Co.*, 380 F. Supp. 2d at 482). Daiichi began conducting tests to establish the safety and efficacy of ofloxacin. (PTX 21 at 203:6-22, 204:4, 204:14-205:9, 205:21-206:14, PTX 218). Changes in auditory brain stem response ("ABR") were measured in guinea pigs, before and after injection of topical ofloxacin otic solution into the middle ear space, and compared to positive and negative controls. (PTX 1 at Col. 2, line 30-Col. 3, line 34, Col. 4, lines 14-38; PTX 21, 75:19-76:5, 80:7-10, 80:18-81:16; Trial Tr. Klein, Vol. 2, 3:13-21, 5:14- 12:15). The experimental ABR results showed that topical administration of ofloxacin into the middle ear of guinea pigs caused essentially no ototoxicity; reduction in acoustic acuity (hearing threshold) was also negligible and comparable to the physiological saline negative control. (PTX 1 at Col.2, lines 48-63; Trial Tr. Klein, Vol. 2, 3:13-21, 5:15-12:15, 13:11-14:7).

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staphylococci aureus and staphylococci epidermis. (DTX 17 at D0379).

[14] Amoxicillin was the most common antibiotic used to fight bacterial ear infection during the period from 1987 to early 1988. Trial Tr. Dohar, Vol. 7, 12:12-14.

In contrast, the 4% gentamicin positive control solution administered into the middle ear of guinea pigs caused substantial damage to the hair cells of the cochlea, while the 0.5% ofloxacin solution caused little or very minimal damage. (PTX 1 at Col.4, lines 39-58; Trial Tr. Klein, Vol. 2, 12:3-15). Very little difference was observed in the animals receiving 0.5% ofloxacin solution relative to animals receiving physiological saline control, in terms of seeing no change in the cochlear hair cells of the inner ear, using scanning electron micrographs. (PTX 1, at Col. 4, lines 39-44; Trial Tr. Klein, Vol. 2, 8:6-9; 16:22-18:2).[15]

The '741 patent inventors also tested the ofloxacin concentrations in the middle ear mucosa of the animals receiving 0.5% ofloxacin solution to determine whether durable concentrations of drug are achieved at the site of infection in order to have an antibacterial effect. (PTX 1 at Col. 3, lines 55-68, Col. 4, line 67—Col. 5, line 55 (*see* Table 3 et seq.); Trial Tr. Klein, Vol. 2, 19:12-20:6). The concentration levels of ofloxacin in the middle ear mucosa measured by the inventors showed persistence of the drug at the site of infection. (PTX 1 at Col. 5, lines 1-55—*see* Table 3 et seq.; Trial Tr. Klein, Vol. 2, 27:25-28:25). The inventors also demonstrated very limited tissue distribution of the drug outside of the middle ear mucosa, thereby establishing the minimal risk of systemic toxicity from the topical otic administration of ofloxacin. (PTX 1 at Col. 5, line 34-Col. 6, line 1; Trial Tr. Klein, Vol. 2, 19:12-27:13).

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[15] Scanning electron microscopy is a sophisticated microscopic technique used to get minute details of tissue. (Trial Tr. Klein, Vol. 1, 128:21-23).

The inventors demonstrated that the Minimum Inhibitory Concentration ("MIC") of ofloxacin necessary to inhibit or kill 80% of bacterial strains isolated from patients with middle ear infection was very low (1.56 ug/ml), and their data established that achievable concentrations of ofloxacin at the middle ear mucosa (site of infection) are substantively higher than the 1.56 ug/ml concentration required to inhibit or kill 80% of the microorganisms that might be present at the site of infection. (PTX 1 at Col. 6, lines 5-29—*see* Table 4 et seq.; Trial Tr. Klein, Vol. 2, 29:1-30:10, 33:4-35:12).

The topical otic administration of ofloxacin was confirmed to be safe, in terms of hearing and morphology of (lack of damage to) the cochlear hair cells as measured by ABR and scanning electron microscope, and efficacious for treating bacterial ear infections, in terms of getting a substantive amount of drug at the site of infection compared to what is necessary to inhibit or kill the organism causing the infection. (Trial Tr. Klein, Vol. 2, 35:13-25). The results of the safety and efficacy studies led to the filing of the priority patent application in Japan and the '741 patent application in the United States. (PTX 1 at 2, left column; PTX 6; PTX 6A).[16]

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[16] Daiichi filed the original patent application for the '741 patent with the United States Patent and Trademark Office ("PTO") on April 4, 1989. (DTX 17 at D0013-D0015; Trial Tr. Smith, Vol. 35:1-11). As discussed above, the '741 patent claims priority from Japanese Patent Application No. 86378/88, filed in Japan on April 8, 1988. (PTX 1 at 2, left column; PTX 6; PTX 6A; Trial Tr. Vol. 2, 102:16-18). The application which matured into U.S. Patent '741 was filed on April 12, 1993. That application is a continuation of application Ser. No. 892,740 filed on June 1, 1992, which is a continuation of Ser. No. 622-121, filed on Dec. 1990, which is a continuation of Ser. No.

C. Apotex's ANDA Application

In early 2000, Ms. Anita Hui of Apotex, Inc. was assigned the task of preparing an ofloxacin otic solution formulation that was identical to Daiichi's FLOXIN® Otic. (Trial Tr. Vol. 2, 103:2-5). Ms. Cihua Yang, a formulation supervisor at Apotex Inc., instructed one of her formulation chemists, Mohammed Kabir to test FLOXIN Otic and formulate a generic ofloxacin otic solution product (PTX 19, 12:20-13:18; PTX 23, 17, 15-18:13).

At the beginning of the ofloxacin otic solution project, Apotex obtained samples of Daiichi's FLOXIN® Otic branded product. (PTX 19, 16:19-24; PTX 23, 16:5-17:19). The samples of Daiichi's FLOXIN® Otic were in a box, which stated "FOR USE IN EARS ONLY," and directed the reader to the package insert for "indications, directions and precautions." (PTX 66 at A003237- 38; PTX 76 at A003249; PTX 23, 16:13-23).

Ms. Yang reviewed the indications for use of FLOXIN® Otic at that time (PTX 23, 17:7-14). Mr. Kabir obtained the Physicians Desk Reference edition 54 entry for the FLOXIN® Otic product, which describes FLOXIN® Otic's formulation ingredients and indications for use.

On April 28, 2000, Ms. Yang asked Mr. Kabir to test the physical parameters of Daiichi's FLOXIN® Otic product. (PTX 66 at A03236; PTX 23, 17:15-18:7; PTX 18, 66:8-13). Mr. Kabir tested the content, delivery volume, headspace, density, pH, osmalarity, viscosity, surface tension, color, solid content and water content

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332,913, filed April 4, 1989. (DTX 17 at D0376; Trial Tr. Smith, Vol. 5, 24:11- 28:19).

of Daiichi's FLOXIN® Otic on May 2-4, 2000. (PTX 66; PTX 23, 28:5-39:20). Ms. Yang then instructed Mr. Kabir to formulate the first batch of generic ofloxacin otic solution, 0.3% on May 17, 2000, in accordance with the composition of Daiichi's FLOXIN® Otic, as recited in the Physicians Desk Reference, 54th edition, and to compare its physical parameters with samples of Daiichi's FLOXIN® Otic product. (PTX 67 at A003094; PTX 78 at p. 951 -"Description"; PTX 18, 66:19-68:11; PTX 19, 35:16-37:17; PTX 23 18:8-13).

The formulation work on the generic ofloxacin otic solution, 0.3% was completed by July 10, 2000, one month after Ms. Yang and Mr. Kabir began their formulation efforts by preparing the first 500 ml batch of generic ofloxacin solution. (PTX 19, 74:9-75:19). On October 25, 2002, Apotex submitted ANDA No. 76-527 for Ofloxacin Otic Solution, 0.3% to the FDA. (PTX 47 at p. A00001 and A000057; PTX 17, 25:3-20, 27:12-16, 19-20, 27:23- 28:14). Section IV of Apotex's ANDA No. 76-527, entitled "Comparison Between Generic Drug and Reference Listed Drug," sets forth a chart comparing Apotex's generic ofloxacin otic solution, 0.3% to Daiichi's FLOXIN® Otic solution. (PTX 47 at A000108; PTX 17, 37:4-43:18).

The comparison demonstrates that the archive and other ingredients, route of administration, dosage form and strength, and conditions of use (treatment indications) for Apotex's ofloxacin otic solution, 0.3% are identical to Daiichi's FLOXIN® Otic. (PTX 47 A000108; PTX 17, 37:4-43:18). Section IV of Apotex's ANDA No. 76-527 also makes a side-by-side comparison of its proposed package insert for generic ofloxacin otic solution, 0.3% and the package insert for FLOXIN® Otic, in which Apotex's proposed methods

of treatment ("Indications and Usage" and "Dosage and Administration") are identical to the FDA-approved methods of treatment for Daiichi's FLOXIN® Otic. (PTX 47 at A000087-88, A000095-96 and A000098-108; *cf.* Daiichi's "Indications and Usage", "Dosage and Administration" and "Medication Guide" to Novex Pharma's (Apotex's) "Indications and Usage", "Dosage and Administration" and "Medication Guide"; PTX 17, 40:25-41:16; *see also* PTX 7C and PTX 78).

Apotex's proposed "Indications and Usage" for generic ofloxacin otic solution, 0.3% in its original ANDA submission are: (i) Otitis Externa in adults and pediatric patients, one year and older; (ii) Chronic Suppurative Otitis Media in patients 12 years and older with perforated tympanic membranes; and (iii) Acute Otitis Media in pediatric patents one year and older with tympanostomy tubes caused by the designated microorganisms. (PTX 47 at A000088 and A0001321 PTX 17, 32:13-33:23).

On June 2, 2004, Apotex submitted a Gratuitous Labeling Amendment to the. FDA, "'carving out" (eliminating) thc Otitis Externa indication, leaving Chronic Supportive Otitis Media in patients 12 years and older with perforated tympanic membranes and Acute Otitis Media in pediatric patients one year and older with tympanostomy tubes as the treatment indications for which it seeks FDA approval. (PTX 39 at A006864, A006883, A006891, A006895, A006906-6908, A006920 and A006921 PTX 42 at A006846; PTX 16, 40:24-41:24, 45:11-46:2).

Apotex concedes that the method of administering generic of loxacin otic solution is identical to the '741 patent for Claims 1,2,4,5 and 6, but contends that it has not infringed Daiichi's patent '741 because the patent is invalid as anticipated and obvious based on

prior art and is unenforceable due to Daiichi's inequitable conduct.

II. CONCLUSIONS OF LAW

A. Invalidity of the Patent

A patent issued by the United States Patent Office is presumed to be valid, and the burden of establishing invalidity rest on the party asserting it. *Tokyo Shibaura Elec. Co., v. Zenith Radio Corp.*, 548 F.2d 88, 93 (3d Cir. 1977) (citing 35 U.S.C. § 282 (1970)). Invalidity must be demonstrated by clear and convincing proof. *Universal Athletic Sales Co. v. American Gym, Recreational & Athletic Equip. Corp.*, 546 F.2d 530, 540 (3d Cir. 1976); *see also Merck & Co. v. Teva Pharms. USA, Inc.*, 228 F. Supp. 2d 480, 496 (D. Del. 2002). "Clear and convincing evidence is evidence that places in the fact finder an 'abiding conviction that the truth of (the] factual contentions are highly probable.'" *Merck & Co.*, 228 F. Supp. 2d at 496 (citing *Colorado v. New Mexico*, 467 U.S. 310, 316, 104 S. Ct. 2433, 81 L. Ed. 2d 247 (1984)).

This standard is particularly applicable when it appears that the prior art invoked to invalidate a patent has been considered by the Patent Office. *Universal Athletic Sales Co.*, 546 F.2d at n.28. Apotex claims, however, that Daiichi failed to disclose certain references that are material to this patent infringement suit and argues that the patent is unenforceable because of Daiichi's inequitable conduct. DPFF 107. Apotex further contends that based on the prior art, Daiichi's '741 patent was anticipated and its subject matter was obvious to a person ordinarily skilled in the art.

1. Anticipation

A patent is invalid for anticipation if a single prior art reference discloses each and every limitation of the claimed invention. *Schering Corp. v. Geneva Pharms., Inc.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003) (citing *Lewmar Marine, Inc. v. Barient, Inc.*, 827 F.2d 744, 747 (Fed. Cir. 1987)). When more than one reference is required to assert invalidity of the claimed invention, anticipation under § 102 cannot be found. *Advanced Display Sys., Inc. v. Kent State Univ.*, 212 F.3d 1272, 1282 (Fed. Cir. 2000). There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. *Aventis Pharms., Inc., v. Barr Labs.*, 372 F. Supp. 2d 430, 434-35 (D.N.J. 2005) (citing *Scripps Clinic & Research Found. v. Genentech, Inc.*, 927 F.2d 1565, 1576 (Fed. Cir. 1991)).

A prior art reference may, however, anticipate without disclosing a feature of the claimed invention if that missing characteristic is necessarily present, or inherent, in the single anticipating reference. *Schering Corp.*, 339 F.3d at 1377 (citing *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991)). A prior art reference which expressly or inherently contains each and every limitation of the claimed subject matter anticipates and invalidates. *See, e.g., EMI Group N. Am., Inc., v. Cypress Semiconductor Corp.*, 268 F.3d 1342, 1350 (Fed. Cir. 2001).

Apotex argues that the published German patent application, DE 36 32 222 Al to Grohe ("Grohe '222"), U.S. Patent 4,844,902 to Grohe ("Grohe '902") (collectively "Grohe Disclosures") and Hirota patent 4,923,862 ("Hirota '862") each anticipate the '741 patent. Apotex

sought to establish at trial, through extensive testimony from its expert witnesses, that each element of the claims of the '741 patent is disclosed in the Grohe Disclosures or in Hirota '862. (*See*, e.g., Trial Tr. Robinson, Vol. 4, 3-18, 29-44). The evidence does not support Apotex's position. Although the Grohe Disclosures and Hirota '862 teach certain elements of the claim limitations of the '741 patent, their disclosures are not identical to the '741 patent, nor are the '741 patent's claim limitations inherent in the Hirota or Grohe Disclosures.

Grohe Disclosures

Grohe '222 and Grohe '902 disclose topical preparations of gyrase inhibitors, which are a class of antibacterial compounds. (DTX 17 at D245-49 and D275-292; DTX 21 at Col. 1:6-10 (A6611) and Cols. 17-34 (A6619-6627); Trial Tr. Dohar, Vol. 7, 143:19-144:18). The only difference between Grohe '222 and Grohe '902 is that the topical preparations discussed in Grohe '902 additionally comprise a corticosteroid.[17]

Grohe '222 teaches that ofloxacin is among the group of gyrase inhibitors that can be "applied topically as topical preparations for the treatment or prophylaxis of infections, diseases and injuries of the skin . . . [as well as] deep or systemic infections." (DTX 17 at D0251). Grohe '222 discloses that gyrase inhibitors can be applied in the topical preparations as such or "as salt with an acid base." (*Id.*) Grohe '222 further discusses that the topical preparations can be used in several forms, including solutions. (*Id.* at

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[17] Since all claim limitations of a patent must be contained in a single prior art reference for the patent to be anticipated by that reference and because Grohe '222 and Grohe '902 are essentially the same, only Grohe '222 will be discussed here.

D0252). Claim 1 of the Grohe patent application states that "[a] topically applicable formulation comprising weight about 0.05 to 30% of an antibacterially active compound . . ." should be used. (*Id.* at D0247).

Grohe '222 adds that topical preparations of the invention are especially effective against bacteria and bacteria-like microorganisms, including staphylococci aureus, staphylococci epidermis, streptococci pneumonia, hemophilus influenzae, pseudomonas aeruginosa, which are all bacteria known to cause otitis media and otitis externa. (*Id.* at D0273; *see also* DTX 375, Table 4; *see supra* 12). Furthermore, the Grohe patent application discloses that besides humans, bacterial infections can also be treated in other animals and lists otitis as a bacterial infection that can be treated in dogs and cats. (*Id.* at D0274).

Dr. Joseph R. Robinson, Apotex's expert witness on the design and development of opthalmic preparations and opthalmic drug delivery systems, testified that the element of Claim 1 of the '741 patent disclosing "an amount of Ofloxacin or a salt thereof [safe and efficacious] to treat [bacterial ear infection]" is taught by page D0251 of the Grohe patent application, which states that "gyrase inhibitors [including ofloxacin] can be applied in topical preparations as such or as salt with an acid or base." (Trial Tr. Robinson, Vol. 2, 135:8- 16). The Court does not find these disclosures identical. More specifically, the Court finds that a person ordinarily skilled in the art would not infer from this disclosure or from any other disclosures in Grohe '222 that ofloxacin is safe to treat bacterial ear infections as is taught in Claim 1 of the '741 patent.

Dr. Robinson further testified that the safety of the use of Ofloxacin is indicated by the disclosure of

Grohe '222, which states that "[f]or low toxicity the topical preparation according to the invention show a wide antibacterial spectrum against Gram-positive and Gram-negative germs." (Trial Tr. Robinson, Vol. 2, 137: 5-17; DTX 17 at D0272). He explained that "[t]oxicity is a relative term" which refers to the range at which the concentration of a drug exceeds therapeutic effectiveness and becomes toxic. (Trial Tr. Robinson, Vol, 2, 138:21-23). Robinson stated that an agent that has low toxicity generally has a low lethal dose and low sensitization, photosensitization or antigenicity.[18] (*Id.* at 138:13-20; 139:5-8).

Dr. Hain, Apotex's expert witness testifying in the field of neurology and ototoxicity, explained that Grohe's discussion of the systemic toxicity of Ofloxacin concerned how much Ofloxacin would be needed in order to kill a mouse. (Trial Tr. Hain, Vol. 3, 43:19-21). He clarified that photosensitization regards whether a preparation put on the skin becomes more vulnerable to the sun, which is not relevant to the treatment of the external ear cavity. (*Id.* at 43:1-3). He added that antigenicity meant that "people do not become allergic to that preparation." (*Id.* at 43:12-14). As discussed below, these concerns are not equivalent to the hearing loss and tissue distribution safety concerns that affect the ear. (*See infra* at 29-30).

Dr. Robinson further maintained that Claim 6 of the '741 patent, which refers to an "aqueous solution of ofloxacin being applied to the external auditory

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[18] Grohe actually does not reference sensitization, photosensitization or antigenicity. These terms are, however, discussed in the Hirota patent application. (PTX 28 at A006609).

canal by instillation," is "intuitively obvious." (Trial Tr. Robinson, Vol. 2,'149:3). He testified that Claim 6 merely refers to the instillation of a dosage unit or drop into the ear to treat an ear infection and is present in any application that discusses topical administration, especially in a solution form. (*Id.* at 3-17). He noted that Grohe '222 "mention[s] the term solutions . . . on D0252" and water being used with solutions on D0270. (*Id.* at 147:18-19; 148:8-1:5). He further testified that Grohe '222 teaches that "[t]he present invention also includes pharmaceutical preparations in dosage units," and that the invention can be used to treat otitis in dogs and cats. Based on all of these disclosures, Robinson concluded that Grohe '222 clearly discloses that an ear drop is instilled into the ear as taught by Claim 6 of the '741 patent.

The Court is not persuaded by Apotex's piecemeal attempt to show that the Grohe '222 is identical to the '741 patent. The Court finds that a person ordinarily skilled in the art would not have concluded based on the several sections of the Grohe patent application relied on by Apotex, that Grohe '222 teaches the safe and efficacious treatment of ofloxacin topically administered to the ear prior to April 8, 1988. *Glaxo Group Ltd. v. Teva Pharm. USA, Inc.*, C.A. No. 02-219 GMS, 2004 U.S. Dist. LEXIS 16750, at *36 (D. Del. August 20, 2004) ("Drawing this conclusion . . . requires several leaps, which the court finds would not have been taken by a person of ordinary skill in the art on or before June 25, 1985").[19] Cherry picking

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[19] Grohe '222 further teaches that the gyrase inhibitors can be used to treat injuries of the skin. (DTX 17 at D0251). Robinson testified that the external auditory canal is skin, but noted that the skin right on the outside of the ear has some differences in

sections from different pages of the Grohe '222 patent application that are not necessarily related, does not satisfy Apotex's burden to show by clear and convincing evidence that Grohe '222 anticipates the '741 patent.

To render a patent invalid, an anticipating reference must describe the patented subject matter with sufficient clarity and detail to establish that the subject matter existed and that its existence was recognized by persons of ordinary skill in the field of the invention. *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534, 545 (Fed. Cir. 1998). Anticipation is not established if it is necessary to pick, choose and combine various portions of the disclosure not directly related to each other by the teachings of the reference in order to show that the claims of the patent at issue are identically disclosed in the prior art. *Application of Arkley*, 455 F.2d 586, 587-88 (Cust. & Pat. App. 1972) ("Such picking and choosing may be entirely proper in the making of a 103, obviousness rejection . . . but it has no place in the making of a 102, anticipation rejection."). Therefore, Apotex has failed to show by clear and convincing evidence that Grohe '222 anticipates the '741 patent.

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the composition of the glands that constitute the tissue inside the external ear canal. Robinson nevertheless concluded that the external auditory canal is "basically an extension of the skin." (Trial Tr.' Robinson, Vol. 4, 13:15-17). This testimony exemplifies the types of analytical leaps continuously made by Apotex. Such analytical leaps are not sufficient to satisfy Apotex's burden. *Glaxo Group Ltd.*, C.A. No. 02-219 GMS, 2004 U.S. Dist. LEXIS 16750, at *1 (prior art establishing that drug could be used to treat migraine did not anticipate method of using drugs to treat nausea and emesis, which were symptoms of migraines).

Hirota 1862

The Hirota '862 patent, entitled "Topical Preparation Containing Ofloxacin," was filed on December 17, 1987 and was issued May 8, 1990. Hirota teaches that ofloxacin, which was disclosed as an "excellent antimicrobial agent" in the Hayakawa '892 patent, had been chiefly administered as an oral agent. (DTX 28 at A006607, Col. 1, lines 16-18). Hirota discloses, however, that ofloxacin or its optical isomer also can be utilized as topical preparations. The claims of the Hirota patent are directed to topical hydrogel or oil-in-water cream preparations containing ofloxacin or "a pharmaceutically acceptable salt thereof." (DTX 28).

A variety of dose forms and bases can be applied to the topical preparations according to the Hirota patent. Hirota discloses, however, that hydrogels and creams are superior in absorbability to general ointments that use vaseline or other bases, which have low percutaneous absorption. (*Id.* Col. 1, lines 50-58). Percutaneous absorption describes a drug's absorption through the skin into the blood for preparations such as opthalmic ointment preparations. (Trial Tr. Hain, Vol. 3, 60:23-61:12; DTX 28 at A006607, Col. 1, lines 59-61). The Hirota patent teaches, however, that its inventions do not always require percutaneous absorption.

Hirota '862 discloses that the topical preparations of the invention are administered by directly applying an appropriate amount to the affected part, or spread on sterilized gauze and attached to the skin. The patent identifies several bacteria that the invention exhibits potential antimicrobial activities on, including staphylococcus, streptococcus pyogenes, pseudomonas aeruginos, heomophylus influenza, bacteria

known to cause otitis media and otitis externa, noting that the invention is expected to produce "excellent therapeutic effects on skin diseases caused by these microorganisms." (DTX 28 Col. 6, lines 10-21).

Like it does with Grohe '222, Apotex picks and chooses elements of Hirota in an effort to invalidate the '741 patent on the basis of anticipation. Hirota, unlike Grohe '222, does not even disclose the treatment of otitis in dogs and cats, but states that the topical preparation of ofloxacin, in hydrogel and oil-in-water cream preparations, was useful for treating and preventing infection in nasal or auricular cavities. *Id.* The Court does not credit Robinson's testimony that the auricular cavity includes the external auditory canal (Trial Tr. Robinson, Vol. 4, 38:1). Even if the Court did accept this opinion, a person of ordinary skill in the art would not know from the Hirota disclosures that the topical preparation of ofloxacin is useful, let alone safe, for the treatment of bacterial ear infections. Therefore, Apotex has not shown by clear and convincing evidence that Hirota anticipates the '741 patent.

Lack of Ototoxicity Disclosure

Apotex notes, and the Court agrees, that the claims define the invention, and it is the claims, not the specifications, that are anticipated. *Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560, 1571 (Fed. Cir. 1988). Based on that proposition, Apotex argues that the fact that Grohe and Hirota do not discuss "ototoxicity" does not preclude anticipation because "ototoxicity" is not an element of the claims in the '741 patent. (*See* Defendants PCL 109). Although the claim limitations of the '741 patent do not expressly state the word ototoxicity, they disclose "a method for treating otopathy which comprises the

topical otic administration of an amount of ofloxacin or a salt thereof 'effective' to treat otopathy." (DTX 375 at D0379, Col. 6, lines 36-39). The Court has construed the word "effective" to mean safe and efficacious finding that "[s]afety was a paramount concern of the inventors" of the '741 patent. *Daiichi Pharm. Co.*, 380 F. Supp. 2d at 488.

Grohe '222 discloses nothing regarding the safe topical otic administration of an amount of ofloxacin to treat otopathy. Although Hirota teaches that the topical hydrogel and cream preparations, when applied to the skin, did not cause any problems of antigenicity, skin sensitinogenicity, and photo sensibilisinogenicity, these are not the paramount safety concerns that are at issue when discussing otopathy. *See supra* 25. Ototoxicity and minimal tissue distribution in the blood serum, central nervous system and inner ear perilymph are. Therefore, unlike the *In re Aventis Pharms., Inc.* case cited by Apotex to support its position, the Court finds that the safe topical administration of ofloxacin is a claim limitation that is imparted by the characteristics or properties of the patent. *Cf.* 372 F. Supp. 2d 430, 439 (D.N.J. 2005) (concluding that the presence of a separate intragranular disintegrant which is distinct from a tablet without a separate intragranular disintegrant was not a claim limitation and could not preclude a finding of anticipation). Since Apotex has provided no evidence that Grohe or Hirota disclose the safe, nonototoxic topical use of ofloxacin, it has failed to meet its burden of proof.

2. Obviousness

A patent may be deemed invalid if it is "obvious." Under 35 U.S.C. § 103, "(a) patent may not be obtained . . . if the differences between the subject

matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which the subject matter pertains." Put simply, an invention is invalid if "the difference between the new thing and what was known before is not considered sufficiently great to warrant a patent." *Glaxo Group Ltd.*, 2004 U.S. Dist. LEXIS 16750, at *29 (citing *Graham V. John Deer Co.*, 383 U.S. 1,15, 15 L. Ed. 2d 545, 86 S. Ct. 684 (1966)) In *Graham*, the Supreme Court established three criteria that the courts must consider to determine whether a patent is obvious: 1) the scope and content of the prior art, 2) differences between prior art and claims at issue and 3) the level of ordinary skill in the pertinent art. 383 U.S. at 17-18; *see also Universal Athletic Sales Co.*, 546 F.2d at 541. The Supreme Court further set forth permissive or secondary criteria that courts should weigh in determining whether a patent is obvious, including commercial success, long felt but unsolved needs and failure of others. *Graham*, 383 U.S. at 17.

Apotex argues that based on the prior art and in particular, Grohe '222, Hayakawa '892, Hirota '862, Katz '456, and the Ganz article[20] and the two Lenarz articles,[21] patent '741 is obvious. Daiichi maintains that none of these materials disclose the topical otic administration of ofloxacin for the safe and effica-

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[20] Ganz, H. "Gyrase inhibitor in local treatment of chronic bacterial, infection in radical middle ear cavities," (1986) H.N.O. (West Germany) 34:511-514.

[21] *See* Lenarz, T. "Chemotherapy of Otitis Media with Ofloxacin" (1987) Drugs 34:139-143 (supp. 1); Lenarz, T. "Ofloxacin in Oral Chemotherapy of Acute and Chronic Otitis Media" (1986). Infection 14:s324-326.

cious treatment of otopathy or bacterial ear infections. The Court agrees.

First, the Hayakawa '892 patent only discloses the compound ofloxacin.[22] Although Apotex suggests that Daiichi merely seeks to extend the Hayakawa '892 patent, Hayakawa did not disclose the topical otic administration of an amount of ofloxacin safe and efficacious to treat bacterial ear infection. (*See* Trial Tr. Vol. 1, 62:22-63:14). Second, as discussed earlier, neither Grohe '222 or Hirota '862 teach that the topical administration of ofloxacin to the ear is safe.

Third, U.S. Patent No. 4,551,456 ("Katz '456 patent") was issued November 5, 1985 and described the treatment of a wide variety of bacterial eye infections by the topical administration of norfloxacin and related antibiotics such as ofloxacin. (DTX 17 at D0065, Col. 1, lines 15-18, 31). The patent examiner rejected the '741 patent five times based on the Katz patent, reasoning that Katz '456 teaches that ofloxacin "is effective against a broad spectrum of gram positive and gram negative organism[s]" and can be topically administered to treat bacterial infections including those in the ear. (DTX 17 at D0055, 00085-86, 00190-91, 00294-95, D0333-34).[23]

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[22] Specifically, the '892 patent teaches that compounds [including ofloxacin] "are effective anti-bacterial agents for treatment against various infectious diseases such as urinary tract infections or infections in respiratory organs in mammals including humans." (DTX 17 at D0063, column 12, lines 10-13). It further notes that although the compounds are used normally by oral administration, they can be administered by injection or by "external application depending upon the type of diseases to be treated." (DTX 17 at D0055 and D0063, Col.12:13-17).

[23] In the first rejection, the examiner actually denied the '741 patent application, which consisted of only one claim: "[a] topical

Katz, like Hayakawa, Grohe and Hirota, may have disclosed that the topical otic administration of ofloxacin would be effective to treat otopathy, however, it did not teach that ofloxacin could be topically administered to the ear to treat otopathy safely. This distinction may seem minor, however it is critical in this case where the Court specifically construed the word effective in the '741 patent to mean "safe and efficacious." *Daiichi Pharm. Co.*, 380 F. Supp. 2d at 488.

For instance, Daiichi submitted a declaration in response to the fourth of the five rejections by the patent examiner. Daiichi explained that Katz could not be used to reject the '741 patent because while there is only a small increase in clinical effect between oral versus topical administration of ofloxacin to treat the eyes, studies showed a large increase in the clinical effect when using topical administration of ofloxacin to treat the ears versus oral administration. (DTX 17 at D0300-302). Nevertheless, the patent examiner rejected the '741 patent a fifth time stating that "the declaration shows a comparison of oral vs topical administration but the Katz patent teaches topical administration." (DTX 17 at D0333).

The patent examiner, however, allowed Daiichi's '741 patent to issue after Daiichi submitted its request for reconsideration dated September 26, 1994. This request not only discussed the distinction between the efficacy of oral versus topical administration of ofloxacin in the eyes and ears, but also disclosed the reduction in side effects, especially hearing

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preparation for treating otopathy which contains ofloxacin or a salt thereof as an active ingredient as disclosed" as anticipated by Katz. (DTX 17 at D0055).

toxicity, of the drug and the distribution of the drug to the affected area in adults and children based on the tests conducted by the inventors.

Although the patent examiner never stated explicitly why he allowed the '741 patent to issue, he noted on the form issuing the patent that "this communication is responsive to [Daiichi's] 9-26-94 [request for reconsideration]" (DTX at D0368). Apparently, something in the September 26, 1994 request for reconsideration convinced the patent examiner to change his mind after five rejections; the Court is persuaded that the lack of any disclosure regarding the safety of ofloxacin topically applied to the ear in Hayakawa, Grohe, Hirota or Katz prevents this Court from finding that the '741 patent was obvious.

Similarly, the other articles and documents relied on by Apotex do not disclose the safety element of the patent. In the Lenarz 1986 article titled "Ofloxacin in Oral Chemotherapy of Acute and Chronic Otitis Media," Lenarz discusses a clinical study performed to evaluate the efficacy and safety of ofloxacin through oral administration to middle ear infections. (DTX 50 at S 324). Lenarz noted that ofloxacin caused a very low rate of adverse effects, especially recognizing the absence of ototoxicity. (*Id.* at S 326). The article, however, did not mention the topical administration of ofloxacin to treat bacterial ear infections.

Daiichi submitted the Lenarz 1986 reference to the Patent Office Examiner during the examination of the '741 patent application, but Daiichi did not include a copy of the article written by Lenarz in 1987. (DTX 17 at D109; number 4 "INFECTION, Vol. 14, Suppl. 4, 1986" is Lenarz 1986; *see also* DTX 60). This article is a later version of the Lenarz 1986 article. In contrast to the Lenarz 1986 article, how-

ever, the Lenarz 1987 article ends by stating that "[e]ardrops containing ofloxacin should also be tested for the efficacy and possible ototoxicity." (Trial Tr. Hain, Vol, 3, 86:18-21; DTX 60 at 142).

Apotex itself admits that the last sentence of the Lenarz 1987 article "expressly suggest[ed] to *try* Ofloxacin as an ear drop." DPFF 66(d)(emphasis added). "Obvious to try" is not the standard for obviousness and has long been held not to constitute obviousness. *In re Roemer*, 258 F.3d 1303, 1310 (Fed. Cir. 2001).

> An "obvious-to-try" situation exists when a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued.

In re Eli Lilly & Co., 902 F.2d 943, 945 (Fed. Cir. 1990).

The Court is persuaded by Dr. Dohar, Daiichi's rebuttal expert witness, who testified that Lenarz was "pointing out the very real difference between an oral systemic administration and a topical administration" when he commented that eardrops containing ofloxacin should be tested for ototoxicity. (Trial Tr. Dohar, Vol. 7, 17:10-12). Dr. Dohar further testified that "[Lenarz] understands primarily the fact that with topical administration, there would be a much higher concentration of antibiotic that would be exposed to the ear." (*Id.* at 1712-15).

The Court finds that a person ordinarily skilled in the art would not conclude from the Lenarz article

discussing the safety of oral or systemic ofloxacin that topically administered ofloxacin would be safe to treat bacterial ear infections. Furthermore, a person ordinarily skilled in the art would learn from the Lenarz article that topically administered ofloxacin to the ear must be tested to determine its safety.

Lenarz, nor any other prior art cited by Apotex, contains tests that confirm ofloxacin's safety when applied topically to the ear, which this Court finds is necessary to prove by clear and convincing evidence that the '741 patent is obvious. *See Chiuminatta Concrete Concepts, Inc., V. Cardinal Indust. Inc.*, 145 F.3d 1303 (Fed. Cir. 1998) (Patent which claimed method of cutting concrete at time before concrete had reached specified range of hardness was not invalid for obviousness absent evidence establishing that tests-described in report providing recommendations for' cutting highway concrete-were indicative of work that existed in the prior art.).

Furthermore, in the Question/Answer portion of the Lenarz article, Lenarz was asked to compare a locally administered quinolone such as ofloxacin with other locally applied drugs. Lenarz responded that "[s]ubstances that are effective against Pseudomonas, particularly gentamicin and neomycin, tend to cause ototoxicity. This has not been a problem in or experience with *oral* Ofloxacin." (DTX 60 at 142) (emphasis added). Again, Lenarz's statement focused solely on the safety of oral ofloxacin and supported Daiichi's contention that ototoxicity caused by drugs available to treat bacterial ear infections at the time was a concern of physicians. Lenarz further stated in response to that question that "in otitis externa, the infection is localized under the skin and it is not treatable with ear drops," actually "teaching away"

from the '741 patent. (DTX 51 at 142-43; Trial Tr. Dohar, Vol. 7, 23:19-24:10).

A prior art reference that "teaches away," or discourages the practice of the invention, supports the nonobviousness of the invention. *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994). The Ganz article also relied upon by Apotex, teaches away from the '741 patent. The article, which was written in German but has an English abstract, describes a clinical study of patients suffering from chronic bacterial ear infections (18 infected radical cavities, 2 external otitis) that were treated with a gyrase inhibitor (Ciprofloxacin) solution. (DTX 52 at DSK-01 00635; DTX 17 at D0422). The bacterial infections were cured in 17 out of 20 cases in the study. (*Id.*).

Although Ganz does not mention ototoxicity, he reports that no side effects were seen. (*Id.*). Ganz also notes, however, that gyrase inhibitors such as Ciprofloxacin are antibiotics of second choice. Ganz adds that for local treatment in the ear gyrase inhibitors "should be used only in difficult cases and exclusively by the otologist." (*Id.*). Therefore Ganz's disclosure does not support Apotex's argument that a person ordinarily skilled in the art would know that the use of ofloxacin, a gyrase inhibitor, to treat bacterial ear infections topically is both efficacious and safe.[24]

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[24] Apotex makes two additional arguments that the Court finds are not persuasive. Apotex contends that physician's use of eye drops in the ears prior to April 8, 1988 and the use of ofloxacin tablets for oral ear infections anticipate and make obvious the '741 patent. Apotex claims that a person of ordinary skill in the art would have known ofloxacin was known to be safe in the ear because it was safe for use in the eye according to the product sheet for TARAVID® (ofloxacin) Eye Drops. See DPFF 56 (citing DTX 17 at 405-06). Apotex further contends

As discussed above, safety is an element of the '741 patent claims. The Ganz article cited by Apotex stresses the safety concerns of using gyrase inhibitors. The Lenarz 1987 article also clearly states that studies should be conducted in order. to test the ototoxicity of administering ofloxacin topically to treat otitis media. Furthermore, neither Hayakawa, Katz, Hirota or Grohe establish the safety of treating otopathy topically. The Court, therefore, finds that Apotex has

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that doctors had been using eyedrops to treat ear infections for years. See DPFF 17-19, 56, 103. First, as Dr. Kitahara, one of the patent inventors, noted, even if physicians were using eye drops for use in the ear, they did so off-label, without the support of any safety studies and thus at the risk of impairing their patients' hearing. (DTX 195, Kitahara 11/13/03 Dep. at 227:20-24; 233:21-234:10; 234:24-235:11, 236:18-21, 237:11-240:17). Second, Apotex must show by clear and convincing evidence that the Taravid product sheet was publicly available to a person of ordinary skill in the art prior to the critical date of the invention for it to be considered prior art. *Makurkar v. C.R. Bard, Inc.*, 79 F.3d 1572, 1578 (Fed. Cir. 1996) ("Bard must persuade the trier of fact by clear and convincing evidence that the Cook catalog was published prior to Dr. Makurkar's invention date."). Apotex has not shown by clear and convincing evidence that the product sheet for TARAVID® Eye Drops was ever even published, let alone that it was made publicly available prior to the April 8, 1988 critical date. (DTX 17 at 400-06; DTX 54 at DSK-01 44-45). In addition, ofloxacin eye drops were not approved for use in the United States until 1993. (Trial Tr. Robinson, Vol.4, 98:14- 99:24). Furthermore, Apotex cannot rely on the use of ofloxacin tablets in Japan to strengthen its argument that ofloxacin was safe for use in the ear. "Knowledge or use of a device in a foreign country, such as Russia, without such knowledge or use in this country, is not a statutory bar to the patent in suit." *Badowski v. United States*, 164 F. Supp. 252, 255 (Ct. Cl. 1958). Ofloxacin tablets have yet to be approved for use in the United States. (Trial Tr. Klein, Vol. 2, 43:22-44:2).

not proved by clear and convincing evidence that the '741 patent is invalid for obviousness.[25]

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[25] Secondary considerations further support the Court's finding that the '741 patent is non-obvious. *Trio Process Corp. v. L. Goldstein's Sons Inc.*, 461 F.2d 66, 70-73 (3d Cir. 1972) ("Such secondary considerations as commercial success, long felt but unsolved needs and failure of others, etc. might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented."). The evidence shows that Daiichi's FLOXIN® Otic product was commercially successful considering that its market share increased from 0.1 percent to 20 percent within the first five years. (Trial Tr. Kane, Vol. 8, 59:1, 113:11-19). Further evidence of FLOXIN® Otic's success is demonstrated by the decrease in the market share of Cortisporin® Otic, a drug with name recognition with a brand name sold since 1970 and Cortisporin® Otic's generic equivalents, which declined from about 75-80% to 45% of the ototopical market. (*Id.*, 53:5-9, 126:18-22). The Court finds that '741 patent also satisfied a long felt medical need by providing physicians with a nonototoxic alternative to the available drugs to treat bacterial ear infections. The '741 patent also did not cause the same safety concerns of side effects, bacterial resistance, irritation of the middle ear mucosa and concentration of the drug absorbed in the blood stream, central nervous system and inner ear perilymph as did conventionally available antibiotics. (PTX 139 at DSK-06 9591, left-hand column; DTX 194, Kitahara Dep. (11/12/04) at 109:6-15, 112:2-20; Trial Tr. Klein, Vol. 2, 20:7-21:12). Dr. Hain, Apotex's expert, suggested that ototoxicity was not a critical concern of physicians testifying that physicians used medications that "contained compounds known to have systemic ototoxicity . . . liberally." (Trial Tr. Hain, Vol. 3, 57:2-11). His own expert report, however, states that "ototoxicity associated with the systemic use of aminoglycosides such as Gentamicin has led practitioners to have concerns regarding the risk of ototoxicity from these drugs when applied topically." Id. at 122:19-123:4. Furthermore, Dr. Hain admits that Ofloxacin Otic Solution is safer than Cortisporin Otic Solution and that he recommends using the Ofloxacin Solution instead of ototoxic aminoglycosides whenever possible. *Id.* at 132:22-133:4.

3. Inequitable Conduct

Applicants for patents and their representatives must prosecute patent applications in the PTO with candor, good faith and honesty. *Molins PLC v. Textron, Inc.*, 48 F.3d 1172, 1178 (Fed. Cir. 1995). This duty is codified in 37 C.F.R. § 1.5, which provides that:

> each individual associated with the filing and prosecution of a patent application has a duty of candor and good faith in dealing with the office, which includes a duty to disclose to the Office all information known to that individual to be material to patentability.

A party asserting that an applicant breached the duty of candor to the patent office must show by clear and convincing evidence (a) an intent to mislead and (b) either the concealment of non-cumulative prior art known to be material or an express misrepresentation to the PTO. *Nordberg*, 82 F.3d at 397; *see also Pharmica Corp. v. Par Pharm. Inc.*, 417 F.3d 1369, 1373 (Fed. Cir. 2005). Apotex argues that patent '741 is unenforceable because Daiichi wrote the incorrect date on a form submitted to the examiner disclosing the Grohe application and failed to disclose the Hirota patent, which were both material to the patent examiner's review. Although the documents may have been material to the '741 patent application, the Court rejects Apotex's claim that the patent is unenforceable due to Daiichi's conduct.

Grohe '222

On June 1, 1992, Daiichi submitted to the PTO a copy of Chemical Abstract No. 110 page 29110 for the Grohe '222 reference and an Information Disclosure Statement ("IDS") listing that abstract. (DTX 17 at D0178 and D0186; Trial Tr. Smith, Vol. 5, 162:3-13).

On April 12, 1993, Daiichi submitted the German language original and a full 49-page English translation of Grohe `222 as part of another IDS, in which Daiichi directed the examiner's attention to the disclosure of Grohe '222. (DTX 17 at D0243-292; Trial Tr. Killworth, Vol. 6, 120:10-18).

On the PTO Form 1449 submitted with the IDS, the applicants wrote the incorrect publication date of the Grohe patent application. (DTX 17 D0216). The applicants typed that the German application was published 7/7/88, instead of typing 4/7/88, which was one day before the April 8, 1988 priority date of the '741 patent. (*Id.*). The examiner drew a line through the German patent listing of Grohe '222 on the PTO Form 1449, with the incorrect typed date, signifying that he had not considered the German application in his examination. (Trial Tr. Smith, Vol. 5, 34:5-25). Beside the English translation of the German Patent, however, the examiner initialed the translation representing that he had considered it and dated the listing using the incorrect date that the applicant had typed on the form. (*Id.*). The Government Printing Office then put July 7, 1989, as the publication date for the Grohe patent application on the face of the Daiichi 1741 patent, making yet another mistake as to the publication date of the Grohe patent. (Trial Tr. Smith, Vol. 5, 126:22-127:17; Trial Tr. Killworth, Vol. 8, 19:15- 21:9).[26] Daiichi never took any steps to correct the wrongly listed date. (Trial Tr. Smith, Vol. 5, 108:21-110:5).

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[26] Although it is uncertain why the Government Printing Office put the date as July 7, 1989, the handwritten 7/7/88 date, written by the patent examiner on the 1449 form was somewhat illegible.

Apotex contends that an inference of intent can be drawn from what its expert, Dr. Smith, who had worked at the PTO for 33 and a half years, refers to as Daiichi's "three false representations." (Trial Tr. Smith, Vol. 6, 55:23-24). Smith explains that Daiichi made two false representations when they stated on the IDS that Grohe '222 contains "no disclosure of topical preparations for the ear as *is the case with the present invention*," and does not suggest that solutions can be applied to the external auditory canal or injected intratympanically. (DTX 17 at D0243) (emphasis added). Smith claims that Daiichi made its third false representation by dating the German patent application with the wrong date, typing 7/7/88 instead of 4/7/88.

The Court is not persuaded that Daiichi's statements about the Grohe patent application constitute false representations, which were intended to deceive the patent examiner. Grohe '222 suggests that gyrase inhibitors, which includes ofloxacin, can be used to treat otitis in dogs and cats and that solutions-along with creams, sprays, etc.-are types of dosage forms suitable for topical preparations (which is noted several pages before the statement regarding otitis). (DTX 17 at D0251, D0270, D0274). Grohe's disclosures do not necessarily teach that an ofloxacin solution may be topically administered to the external auditory canal or injected intratympanically to treat bacterial ear infections safely and efficaciously as disclosed in the '741 patent. Not only are Daiichi's statements to the patent examiner justified, but Daiichi is entitled to disagree with Apotex's interpretation of Grohe '222, which is not clear from the face of the patent application.

The Court further does not find that there is clear and convincing evidence that Daiichi intended to mislead the examiner by typing the incorrect date on the IDS. Apotex has not submitted clear and convincing evidence that the typed incorrect date was anything more than a typographical error. (DTX 223, Olexy 12/17/03 Dep. at 160:24-161:23; DTX 17 at D0216). The correct April 7, 1988 date was clearly written on both the German and English translations of the application. (DTX 17 at D0217, D0245; Trial Tr. Smith, Vol 5, 159:22-160:10). The examiner did not draw a line through the English translation of the PTO Form 1449, which indicated that he had reviewed that translation putting him on notice of the correct date. (Trial Tr. Smith, Vol. 5, 34:5-25; *see supra* at 42).[27]

Furthermore, the Chemical abstract submitted by Daiichi had the correct date of the application on it, (Trial Tr. Smith, Vol. 5, 91:11-22, 107:23-108:3; DTX 17 at 00186, D0216). Had Daiichi sought to mislead the examiner, it could have tampered with the date on the Chemical abstract or the German and English translations of the application. Instead, Apotex has shown only that the date on the 1449 form was typed

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[27] The Court is not persuaded by Apotex's contention that the examiner would not have understood the date identified as the "date of disclosure" on the English translation to be the date of publication. (Trial Tr. Smith, Vol. 5, 110:6-117:18). Apotex's speculation into what the patent examiner understood the terms "date of disclosure" to mean does not constitute clear and convincing evidence. *Norian Corp. v. Stryker Corp.*, 363 F.3d 1321, 1329 (citing *Kahn v. General Motors Corp.*, 135 F.3d 1472, 1480 (Fed. Cir. 1998) ("Introspection and speculation into the examiner's understanding of the prior art or the completeness or correctness of the examination process is not part of the objective review of patentability")).

incorrectly, which is not sufficient to meet the high standard of clear and convincing evidence.. *SunTiger Inc. v. Scientific Research Funding Group*, 194 F.3d 1335 (Fed. Cir. 1999)("[a]rgument alone is not enough to meet the high standard of proof needed to justify a finding of invalidity, namely that of clear and convincing evidence.").

Moreover, on June 15, 1993 the examiner stated that he rejected the '741 patent application because Katz '456 made obvious that ofloxacin could be administered topically to treat infections. (DTX 17 at D0294). In that rejection letter, the examiner specifically cited page 31, line 12 of the English translation of Grohe '222, noting that the Grohe patent application shows that ofloxacin is effective for treating otitis. (*Id.*). The examiner did not state that he did or did not deny the '741 patent on that basis; however, his statement proves that he reviewed the Grohe '222 patent application further supporting the Court's finding that there is no clear basis upon which to find that the examiner was misled by the incorrect typed date.

Other than the one incorrect date of the PTO Form 1449, Apotex has not provided any evidence that Daiichi purposely sought to deceive the examiner. Therefore, the Court finds that there is no clear and convincing evidence that Daiichi engaged in inequitable conduct by making false representations.

Hirota '862

On June 15, 1989 Daiichi made a filing in the '741 prosecution that was accompanied by an IDS disclosing two prior (co-pending), but as yet unpublished, U.S. patent applications filed by other Daiichi inventors. (DTX 17 at D0051-D0053; Trial Tr.

Vol. 5, 38:21-23). One of those applications, U.S. Patent Application No. 07/133,975, ultimately matured into Hirota '862. (DTX 28 cover page, left column; Trial Tr. Smith, Vol. 6, 9:1- 17). The patent issued on May 8, 1990. (*Id.*).

Daiichi never disclosed that the Hirota application issued as a patent, which then made it available as prior art. (Trial Tr. Smith, Vol. 5, 62:12-14, 86:2-9, 134:7-13, 135:24-136:11). Moreover, the co-pending patent applications had been sealed when filed to protect their confidentiality. In general, once a patent is issued anything under seal as confidential material would be opened up and would become part of the file history. *Ziegler v. Phillips Petroleum Co.*, 483 F.2d 858, 869 (5th Cir. 1973). Yet, no copies of the Hirota application purportedly submitted by Daiichi with the IDS could be found in the file history. (Trial Tr. Killworth, Vol. 8, 8:11-13). Therefore, there is no clear indication that the Hirota patent application was ever considered by the patent examiner. (*Id.* at 14:19 - 15:4).

Daiichi, however, submitted an additional IDS on February 14, 1992, containing the European version of the 1862 Hirota patent. (DTX 17 at D109-10; Trial Tr. Smith, Vol. 5, 169:3-6). This patent listed the issue date of the U.S. Hirota patent. (*Id.*). Along with that IDS, Daiichi provided the examiner with a European Search Report and European Annex, which specifically pointed to the very page and line of the European version of Hirota that Apotex relies on to make its invalidity argument. (DTX 17 at D0180-82; Trial Tr. Smith, Vol. 5, 169:3-9). In addition, Patent Examiner Jerome Goldberg examined both the applications for the Daiichi '741 and Hirota '862 patents. (PTX 1 at 2; right column; DTX 28, cover

page, right column; Trial Tr. Smith, Vol. 6, 10:20-23, 127:4-11; DTX 29 at DSK-18 00869 - EX - bottom of the page; PTX 466). Certain documents in the file history of patent '741 and '862 indicate that examiner Goldberg was reviewing both applications on dates in close proximity with one another. (DTX 17 at D0054-56; Trial Tr. Smith, Vol. 6, 17:6- 15).

Apotex has presented no clear and convincing evidence to show that Daiichi intentionally failed to disclose the Hirota patent. Daiichi voluntarily submitted an IDS for the Hirota patent application. Although no one could find the document in the file history, Apotex has put forth no evidence that the absence of the document is a result of Daiichi's wrongdoing. Furthermore, the European version of the Hirota '862 patent, which also was disclosed voluntarily by Daiichi, clearly noted that the '862 patent had been issued. These facts, coupled with the evidence that patent examiner Goldberg was reviewing both the '862 and '741 patent applications at the same time,[28] support the Court's conclusion that deceptive intent has not been established by clear and convincing evidence.

B. Infringement

It is an act of patent infringement under the Hatch Waxman Act for a company to seek FDA approval to market a generic version of a patented drug product or method of treatment prior to expiration of the

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[28] Although the Court recognizes that examiner Goldberg likely was reviewing over 150 patents during the same time he was reviewing the Hirota and '741 patent applications, in light of all the evidence Apotex has failed to satisfy its burden of showing that Daiichi intended to deceive the examiner. (Trial Tr. Smith, Vol. 6, 39:2-4).

patent, if the generic version, when marketed, would infringe the patent under an ordinary patent infringement analysis. 35 U.S.C. § 271(e)(2); *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 675 (1990). Apotex agreed to a stipulation that "the method of treating bacterial ear infection by administering generic ofloxacin otic solution, 0.3%, for which Apotex seeks approval in its ANDA No. 76-527, is within the scope of . . claims 1,2,4,5, and 6 [of the '741 patent] and those claims in the '741 patent read on the proposed use described in Apotex's ANDA NO. 76.527." (PTX 313 ¶ 1).

Apotex recognizes that in light of this stipulation, any discussion regarding infringement is irrelevant, because Apotex has essentially conceded that it has infringed patent '741, unless the Court finds that the patent is invalid or unenforceable.[29] *See*, e.g., Defendants' Response to PPCL 25 ("Moreover, the statement [regarding Apotex's infringement of the '741 patent] is irrelevant in light of the parties' stipulation (PTX 313). Finally, there can be no liability for infringement of an invalid claim."). Because the Court already has determined that the

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[29] Apotex, however, has not conceded that it infringes upon Claims 3 and 7 of the '741 patent. Apotex argued that because it amended the indications on its package insert and product labeling in June 2, 2004 to exclude the indication for otitis externa, it has not infringed on Claim 3 of the '741 patent or induced the infringement of that claim. Since Daiichi, withdrew with prejudice its claim that Apotex's ANDA No. 76-527 infringes Claim 3 of the '741 patent, however, Apotex's argument is irrelevant. *See* March 28, 2006 Stipulation; *supra* n.7. Furthermore, Daiichi stipulated that based on the Court's interpretation of Claim 7, Apotex's ANDA No. 76-527 was not within the scope of "the literal language of claim 7 . . . or an equivalent thereof." (PTX 313 at 1 4; *supra* n.7).

'741 patent is not invalid as anticipated or obvious and is not unenforceable due to Daiichi's alleged inequitable conduct, Apotex has infringed the '741 patent.

III. CONCLUSION

For the reasons stated in this Opinion, this Court finds that Daiichi's '741 patent is not invalid as anticipated or obvious or unenforceable for inequitable conduct. Furthermore, the Court concludes that Apotex has infringed claims 1, 2, 4, 5 and 6 of the '741 patent.

An appropriate Judgment accompanies this Opinion.

/s/ William G. Bassler
WILLIAM G. BASSLER, U.S.S.D.J.

Dated: August 1, 2006

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

3cv937 (WGB)

DAIICHI PHARMACEUTICAL CO., LTD. and
DAIICHI PHARMACEUTICAL CORPORATION,
Plaintiffs,

v.

APOTEX, INC. and APOTEX CORP.,
Defendants.

FINAL JUDGMENT ORDER PURSUANT TO
FED. R. CIV. P. 54(b)

This action having come to trial before the United States District Court for the District of New Jersey, the Honorable William G. Bassler, Senior District Judge presiding; the issues having been heard on the cause of action of plaintiffs Daiichi Pharmaceutical Co., Ltd. and Daiichi Sankyo, Inc. (hereafter "Daiichi") against defendants Apotex, Inc. and Apotex Corp. (hereafter "Apotex") alleging that Apotex has infringed claims 1, 2, and 4-7 of United States Patent No. 5,401,741 ("the '741 patent") and on the affirmative defenses and counterclaims I-VI of defendant Apotex alleging the noninfringement, invalidity and unenforceability of claims 1-7 of the '741 patent, Apotex's counterclaims VII-XI having been severed and stayed; and a decision having been rendered on the claims, defenses and counterclaims in accordance with the Opinion and Findings of Fact and Conclusions of Law entered in this matter on August 1, 2006, the Court

hereby expressly ORDERS, ADJUDGES AND DECREES ON THIS 1st DAY OF August, 2006 THAT:

1. There is no just reason for delay, and this Court expressly directs entry of judgment pursuant to Fed. R. Civ. P. 54(b).

2. Judgment is entered in favor of Daiichi against Apotex on Daiichi's claim that Apotex has infringed claims 1, 2, 4, 5 and 6 of the '741 patent.

3. Judgment is entered in favor of Apotex and against Daiichi on Daiichi's claim that Apotex has infringed claim 7 of the '741 patent.

4. Judgment is entered in favor of Daiichi and against Apotex on all of Apotex's affirmative defenses and counterclaims I-VI alleging noninfringement, invalidity, or unenforceability of the '741 patent, Apotex having failed to prove by clear and convincing evidence that claims 1-7 of the '741 patent are invalid or unenforceable.

5. Pursuant to 35 U.S.C. § 271(e)(4)(A), the effective date of any approval of Apotex's Abbreviated New Drug Application No. 76-527 for Ofloxacin Otic Solution, 0.3% shall be a date that is not earlier than the date of expiration of the '741 patent, plus any exclusivity that may be attached pursuant to the rules and regulations of the Food and Drug Administration ("FDA"), and Apotex shall promptly provide notice and a copy of this Final Judgment order to the FDA.

6. Pursuant to 35 U.S.C. 271(e)(4)(B), defendants Apotex, Inc. and Apotex Corp., and each of their officers, agents, servants, employees, successors, assigns, affiliates and attorneys, and those persons in active concert or participation with any of the foregoing are permanently enjoined from engaging in the manufacture, use, offer to sell, or sale within the United States, or importation into the United States, of Ofloxacin Otic Solution, 0.3%, the use of which is covered by claims 1, 2, 4, 5 and/or 6 of the '741 patent.

7. The Clerk shall provide copies of this Final Judgment Order to all counsel appearing in this action.

/s/ William G. Bassler
WILLIAM G. BASSLER
SENIOR UNITED STATES DISTRICT JUDGE

APPENDIX C

DAIICHI PHARMACEUTICAL CO., LTD. AND DAIICHI PHARMACEUTICAL CORPORATION,

PLAINTIFFS,

v.

APOTEX, INC. AND APOTEX Corp.,

DEFENDANTS.

No. Civ. 03-937(WGB).

UNITED STATES DISTRICT COURT,
D. NEW JERSEY.

Aug. 8, 2005.

James P. Flynn, Epstein, Becker & Green, P.C., Newark, NJ, Brian P. Murphy, David Leichtman, Morgan Lewis Bockius LLP, New York City, for Plaintiff.

Adorno & Yoss, LLP, Wayne, NJ, Robert B. Breisblatt, Julie A. Katz, Michael A. Krol, Welsh & Katz, Ltd., Chicago, IL, for Defendant.

OPINION

BASSLER, Senior District Judge.

Plaintiffs are Daiichi Pharmaceutical Co. Ltd., a Japanese drug manufacturer, and its New Jersey-based subsidiary, Daiichi Pharmaceutical Corporation (collectively, "Daiichi"). This lawsuit concerns Daiichi's U.S. Patent No. 5,401,741 (the "'741 patent"), entitled a "Topical Preparation for Treating Otopathy."

Daiichi brings this action against Apotex Inc., a Canadian-based generic drug manufacturer, and its subsidiary, Apotex Corp. (collectively, "Apotex") for

willful patent infringement under the Hatch—Waxman Act, 35 U.S.C. § 271(e)(2), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202, and 35 U.S.C. § 271(a), (b) and/or (c).

Jurisdiction and venue in this district are proper pursuant to 28 U.S.C. §§ 1331, 1338(a), 1391(b), and 1400(b).

This Opinion addresses the proper interpretation of the '741 patent claims.

I. BACKGROUND

Daiichi owns the '741 patent, which was issued by the U.S. Patent and Trademark Office ("PTO") in March 1995.[1] The '741 patent discloses a "Topical Method for the Treatment of Otopathy," and sets forth the following seven claims: [2]

> *Claim 1:* A method for treating otopathy which comprises the topical otic administration of an amount of ofloxacin or a salt thereof effective to treat otopathy in a pharmaceutically acceptable carrier to the area affected with otopathy.
>
> *Claim 2:* The method of claim 1 wherein the said otopathy is otitis media.

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[1] The '741 patent was originally issued to its three inventors, Kiichi Sato, Akira Handa, and Takeji Kitahara.

[2] As its title indicates, the '741 patent is a "method" patent, as compared to a machine, composition, or manufacture patent. One treatise explains: "the 'elements' of a method claim, instead of being structural parts, are, and must be, acts or manipulative steps that are performed upon an article, workpiece, or chemical substance. It is the transformation or reduction of the article, workpiece, or chemical substance to a different state or thing that is the essence of a method claim." Robert C. Faber, *Landis on Mechanics of Patent Claim Drafting* (5th ed.2004) (emphasis in original).

Claim 3: The method of claim 2 wherein the said otopathy is otitis externa.

Claim 4: The method of claim 2 wherein the concentration of ofloxacin in the pharmaceutically acceptable carrier is about 0.05 to about 2% w/v.

Claim 5: The method as claimed in claim 4, wherein the dosage form of ofloxacin is an aqueous solution.

Claim 6: The method as claimed in claim 5, wherein the aqueous solution of ofloxacin is applied to the external auditory canal by instillation.

Claim 7: The method as claimed in claim 6, wherein the aqueous solution of ofloxacin is intratympanically injected through a puncture in the tympanic membrane.

(Declaration of Michael A. Krol in Support of Apotex' Claim Construction Brief ("Krol Decl."), Exh. A.) The '741 patent is not due to expire until March 2012. (Daiichi Brief in Support of Claim Construction ("Daiichi Br."), at 1.)

At the time that Daiichi's researchers began working on the '741 patent, a number of antibiotics were available for the treatment of bacterial ear infections. Unfortunately, these antibiotics, whether administered to patients systemically (by ingestion or injection), or topically (by application to the surface of the infected area), were associated with certain adverse side effects. For example, patients given oral antibiotics, such as amoxicillin, were known to develop bacterial resistance, thereby reducing or eliminating the effectiveness of the antibiotic. (*Id.* at 7.)

Topical administration of antibiotics, while an improvement over systemic administration, presented its own risks.[3] Specifically, when certain antibiotic compounds were applied to the surface of the middle ear they could "migrate" into the inner ear, causing structural damage and resulting in permanent hearing loss and/or impairment of balance—side-effects referred to in the field as "ototoxicity." (*Id.*, at 8-9.)

The risk of ototoxicity is not limited to topical administration of antibiotic compounds directly to the middle ear. Rather, if the compound is applied to the surface of the external auditory canal of patients whose tympanic membranes are ruptured—a condition which can develop in patients with middle ear infections—the drug may migrate first to the middle ear, and then to the inner ear, thereby presenting the same risks of ototoxicity. (*Id.* at 8.)

There are therefore at least two situations which present the risk of ototoxicity. First, when a patient suffers from *otitis media,* a bacterial infection of the middle ear. Second, when *a* patient suffers from *otitis externa,* a bacterial infection of the external auditory canal, with a ruptured tympanic membrane.' This latter situation is particularly troublesome for treating physicians because in many cases of otitis

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[3] To understand these risks, it is helpful to know that the ear consists of three chambers: (I) the outer ear, including the external auditory canal, which focuses sound waves on the tympanic membrane (commonly known as the ear drum); (2) the middle ear, which conducts sound; and (3) the inner ear, which transmits sound vibrations to the auditory nerve for processing into sound. (Daiichi Br., at 4.) The tympanic membrane separates the external auditory canal from the middle ear. *(See* Daiichi Br., at 2-4.)

externs, the swelling of the external auditory canal makes it difficult, if not impossible, to know if the tympanic membrane[4] is intact prior to initiating antibiotic therapy. (*Id.* 4-5.)

The method described in the '741 patent was intended to overcome these risks, by setting forth a method for the topical administration of ofloxacin—a previously known antibiotic compound—to both the external auditory canal and the middle ear, while significantly reducing the risk of ototoxicity and antibacterial resistance. (Krol Decl, Exh. A; Daiichi Br. 8-11.)

In 1997, two years after the issuance of the '741 patent, the Food and Drug Administration ("FDA") approved Daiichi's FLOXIN® Otic product, which is covered by the terms of the '741 patent and is the first antibiotic ear drop approved by the FDA for use in both the external auditory canal and the middle ear. (*Id.,* at 6.)

In early 2003, Daiichi received notice that Apotex, a Canadian-based generic drug manufacturer, had filed with the Food and Drug Administration ("FDA") an Abbreviated New Drug Application ("ANDA") for Ofloxacin Otic Solution. Arguing that Apotex' Ofloxacin Otic Solution is a generic "copy" of its FLOXIN® Otic product, Daiichi filed this suit in March 2003. The amended complaint (the "Amended Complaint"), filed in May 2004, alleges willful infringement of all seven claims of the '741 patent.

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[4] *Otitis* media and *otitis externa* are characterized by localized pain, swelling, and inflammation. *Otitis* externa is commonly referred to as "swimmer's ear." (*Id.*)

Apotex denies Daiichi's allegations and raises the following defenses: (1) patent invalidity; (2) anticipation; (3) obviousness; (4) unenforceability; (5) noninfringement; (6) noninfringement of claim 7; and (7) misuse. In addition, Apotex has filed a counterclaim against Daiichi, which has since been severed from the main action and stayed pending trial on the issue of infringement.

In accordance with Magistrate Judge Madeline Cox Arleo's October 9, 2003 pretrial scheduling order, the parties have now substantially completed discovery, including depositions.

The sole issue currently before the Court is the proper interpretation of the '741 patent claims. The parties have fully briefed the issue and, on July 22, 2005, the Court conducted a Markman proceeding. This Opinion sets forth the Court's conclusions with respect to claim construction.

II. LEGAL FRAMEWORK

[1] There are two steps in a patent infringement action. First, the claims must be properly construed in order to determine their scope and meaning. Second, the claims as properly construed must be compared to the accused device or process. CVI/*Beta Ventures, Inc. v. Tura LP,* 112 FM 1146, 1152 (Fed.Cir.1997), *cert. denied,* 522 U.S. 1109, 118 S.Ct. 1039, 140 L.Ed.2d 105 (1998). As previously mentioned, this Opinion addresses only the first step, which is a threshold issue of law for the court to decide. *Markman v. Westview Instruments,* 52 FM 967 (Fed. Cir.1995) (en bane), aff'd, 517 U.S. 370, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996).

A. Analytical Framework

[2] "It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1311, 2005 WL 1620331, at *4 (Fed.Cir.2005) (internal quotation marks omitted). Accordingly, a court, in construing the terms of a patent, should look first to the language of the claim itself. *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996).

[3, 4] The words of a claim "are generally given their ordinary and customary meaning." *Phillips*, 415 F.3d 1303, 1311, 2005 WL 1620331, at *5 (internal quotation marks omitted). "[T]he ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Id.*

[5] The ordinary meaning of a term cannot, however. be construed in a vacuum; rather, a court must "must look at the ordinary meaning in the context of the written description and the prosecution history." *Medrad, Inc. v. MRI Devices Corp.*, 401 F.3d 1313, 1319 (Fed.Cir.2005). The court does so to "determine whether the inventor used any terms in a manner inconsistent with their ordinary meaning." *Vitronics*, 90 F.3d at 1582.

[6,7] For example, "the specification acts as a dictionary when it expressly defines terms used in the claims or when it defines terms by implication." *Phillips*, 415 F.3d 1303, 2005 WL 1620331, at *13 (internal quotation marks omitted). Similarly, a patent's prosecution history may clarify the meaning of a claim, particularly in light of exchanges between the patent applicant and the PTO. *See Northern*

Telecom, Ltd. v. Samsung Elec. Co., 215 F.3d 1281 (Fed.Cir.2000). Thus, the claim language, the specification, and the patent prosecution history—collectively referred to in patent law as the "intrinsic record"—are the foundation of claim construction analysis and will, in most instances, resolve any ambiguity in a disputed claim term. *Vitronics*, 90 F.3d at 1582-83 ("Such intrinsic evidence is the most significant source of the legally operative meaning of disputed claim language.")

[8] Only in the rare circumstance in which there is still doubt as to the meaning of a claim after the court has examined the intrinsic record, should a court look to extrinsic evidence such as treatises, technical references, and expert testimony, to resolve any doubts or ambiguities. *Id.*, at 1583.

III. DISCUSSION

With these principles in mind, the Court turns first to a discussion of the "ordinary person skilled in the art," and then to an analysis of each disputed claim term.

A. Ordinary Person Skilled in the Art

[9,10] The person having ordinary skill in the art is a hypothetical *person* who is presumed to know all of the relevant art within the field of invention and any analogous technical fields. *See Standard Oil Co. v. Am. Cyanamid Co.*, 774 F.2d 448, 454 (Fed.Cir.1985). The purpose of this standard is to "provide[] an objective basis from which to begin claim

interpretation." [5] *Phillips,* 415 F.3d 1303, 1311, 2005 WL 1620331, at *5.

[11] The Court of Appeals for the Federal Circuit instructs that the ordinary person is not a judge, a layman, a person skilled in remote arts, or the inventor. *Envtl. Designs, Ltd. v. Union Oil Co.,* 713 F.2d 693, 697 (Fed.Cir.1983). Rather, "[a] person of ordinary skill in the art is ... presumed to be one who thinks along the line of conventional wisdom in the art and is not one who undertakes to innovate, whether by patient, and often expensive, systematic research, or by extraordinary insights . . ." *Standard Oil,* 774 F.2d at 454.

In *Envtl. Designs,* the Court of Appeals for the Federal Circuit set forth the following non-exhaustive list of factors for a court to use in ascertaining the level of ordinary skill in the art: (1) the inventor's educational background; (2) the kinds of problems confronted in the art; (3) solutions found previously; (4) the level of sophistication of the technology; (5) the speed of innovation in the art; and (6) the educational level of active workers in the field. 713 F.2d at 696. At the same time, the Court of Appeals noted that these factors may or may not apply to the facts of a given case[6] *Id.* ("Not all such factors may be

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[5] The "ordinary person" standard has been compared to the "reasonable person" standard used in tort law. *See Panduit Corp. v. Dennison Mfg. Co.,* 810 F.2d 1561, 1566 (Fed. Cir.1987).

[6] One commentator has observed that the Federal Circuit has provided very little guidante on how to define the "ordinary person skilled in the art," despite the fact that this issue is central to resolving many patent disputes. Joseph P. Meara, *Just Who Is the Person Having Ordinary Skill* in *the* Art? *Patent Law's Mysterious Personage,* 77 Wash. L. Rev. 267, 268 (2002).

present in every case, and one or more of these factors may predominate in a particular case.").

Here, Daiichi argues that the ordinary person skilled in the art is "a general practitioner or pediatrician of modest experience." (Daiichi Br., at 13.) By contrast, Apotex argues that it is "a physician with detailed understanding of ear diseases, e.g., an otolaryngologist, and a pharmaceutical scientist, such as a pharmacist with an advanced degree (Pharm. D. or Ph.D.), or another worker in the field with expertise in medicinal chemistry and pharmaceutical formulation." (Apotex Moving Brief on Claim Construction ("Apotex Br."), at 11.) Noting that the parties offer little more than conclusory arguments concerning this issue in their briefs, the Court finds that two prior decisions, one issued by the Court of Appeals for the Federal Circuit and one by an Indiana district court, are especially helpful.

The first case, *Merck and Co., Inc. v. Teva Pharm. USA, Inc.*, 347 F.3d 1367 (Fed.Cir.2003), cited by Daiichi, involved a patented method for treating osteoporosis, through the administration of a bisphosphonic acid. At the center of the claim construction dispute was whether the term used to refer to the acid in the patent should be read to encompass the active agent contained in the accused product.

Rejecting the testimony of the defendant's expert witness, a chemist, the Court of Appeals affirmed the district court's conclusion that, in this case, a person skilled in the art would have: (1) a medical degree; (2) experience treating patients with osteoporosis; (3) and knowledge of the pharmacology and usage of bisphos phonates. *Id*, at 1371.

In the second case, *Eli Lilly & Co. v. Teva Pharmaceuticals,* 2004 WL 1724632 (S.D.Ind. July 29, 2004) (unpublished decision), an Indiana district court used similar reasoning. The case involved several patents for the use of fluoxetine, more commonly known as Prozac®, for the treatment of depression and anxiety. Plaintiff sued for patent infringement when the defendant, a generic drug manufacturer, sought FDA approval to sell a generic version of fluexotine for the treatment of premenstrual syndrome ("PMS").

[12] In analyzing the defendant's obviousness defense,[7] the district court stated that, "to limit 'one of ordinary skill in the art' to clinical researchers would be too restrictive." *Id.* The district court went on to conclude that the ordinary person skilled in the art would be a "medical doctor (an OB/GYN, a family practice physician, or a psychiatrist) who: (1) regularly sees and treats patients suffering from PMS; and (2) is familiar with the prior art." *Id.* at *33.

The Court sees no reason why the logic employed in *Merck* and *Eli Lilly & Co.* should not apply to the facts of this case. Here, the ordinary person skilled in the art would have a medical degree, experience treating patients with ear infections, and knowledge of the pharmacology and use of antibiotics. This person would be, as Daiichi argues, a pediatrician or

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[7] A patent claim is invalid under 35 U.S.C. § 103(a) "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." *Velander v. Garner,* 348 F.3d 1359, 1363 (Fed. Cir. 2003).

general practitioner—those doctors who are often the "first line of defense" in treating ear infections and who, by virtue of their medical training, possess basic pharmacological knowledge.

B. Disputed Terms

Having determined that the ordinary person skilled in the art is a person with a medical degree, experience treating patients with ear infections, and knowledge of the pharmacology and use of antibiotics, the Court now turns to the disputed claim terms themselves.

In their briefs filed with the Court, each party submitted a chart setting forth its proposed claim language. After reviewing the charts and observing that the parties disagreed as to almost every term used in the patent, the Court asked the parties to submit a jointly prepared claim construction chart, so as to identify the material terms in dispute. The jointly prepared chart was of limited usefulness and the parties were asked, at the *Markman* proceeding, to identify exactly which terms the Court was being asked to interpret. The parties agreed that the Court need only address the following three terms: (1) "otopathy"; (2) "effective to treat;" and (3) "intratympanically injected through a puncture of the tympanic membrane." The Court addresses each of these three terms in order.

1. "otopathy"

[13] The parties disagree as to the proper interpretation of "otopathy," a term used in Claims 1, 2, and 3 of the patent. Daiichi argues that it should be construed to mean *"otitis externa* and/or *otitis media,"* By contrast, Apotex argues that it should be

construed as "any disease of the ear." The Court does not find either argument persuasive.

[14] The doctrine of claim differentiation requires each claim to have a different scope. As the Court of Appeals for the Federal Circuit explains:

> There is presumed to be a difference in meaning and scope when different words or phrases are used in separate claims. To the extent that the absence of such difference in meaning and scope would make a claim superfluous, the doctrine of claim differentiation states the presumption that the difference between claims is significant.

Comark Comms., Inc. v. Harris Corp., 156 F.3d 1182, 1187 (Fed. Cir. 1998).

Daiichi's proposed construction plainly violates the principle of claim differentiation. Claims 1, with Daiichi's proposed language italicized, reads as follows:

> *Claim 1*
>
> A method for treating *otitis externa and/or otitis media* which comprises the topical otic administration of an amount of ofloxacin or a salt thereof effective to treat *otitis* externa and/or *otitis media* in a pharmaceutically acceptable carrier to the area affected with *otitis externa and/or otitis media*

Such a construction would clearly render Claims 2 and 3 redundant:

> *Claim 2*
>
> The method of claim 1 wherein the said otopathy is otitis media.

Claim 3

The method of claim 2 wherein the said otopathy is otitis externa.

The Court declines Daiichi's invitation to cast aside well-settled principles of claim construction analysis in construing the disputed term.

[15] Rather, the proper course is to adhere to the rule that "[t]he presence of a dependent claim that adds a particular limitation raises the presumption that the limitation in question is not found in the independent *claim.*" *Liebel—Flarsheim Co. v. Medrad, Inc.,* 358 F.3d 898, 910 (Fed. Cir. 2004); *see also Sunroce Roots Enter. Co. v. SRAM Corp.,* 336 F.3d 1298, 1302-03 (Fed. Cir. 2003). Accordingly, the fact that Claim 2 is limited to otitis *media* and Claim 3 to *otitis media* and *otitis externa* persuades this Court that Claim 1 is not limited to *otitis media* and/or *otitis externa*

The Court notes that, at the *Markman* proceeding, Daiichi raised one argument, not previously presented in its briefs, concerning the issue of claim differentiation. The argument is that all of the claims are in fact different under its proposed interpretation because: (1) Claim 2 relates to *otitis media*; (2) Claim 3 relates to *otitis externa*; and (3) Claim 1 refers to otitis media and *otitis externa*. Daiichi's argument simply does not work.

It is well-established that "[c]laims in dependent form shall be construed to include all limitations of the claim incorporated by reference into the dependant claim." *See* 37 C.F.R. § 75(c). Therefore, Claim 3 must be read to include all of the limitations contained in Claim. 2, which would mean that the "otopathy" referred to in Claim 3 is both *otitis externa*

and otitis media, rendering Daiichi's proposed interpretation of Claim 1 redundant.

Daiichi's proposed construction is not only contradicted by the language of the claims themselves, it is also inconsistent with the patent specification as whole. Several sections of the specification explicitly state that *otitis externa* and *otitis media are among* the types of otopathy, *not the only* types of otopathy, to which the '741 patent is directed. For example, the specification states:

> The otopathy on which the preparation of the present invention is effective includes inflammatory otopathy, *such as* otitis media and otitis externa . . .

(Krol Decl., Exh. A (emphasis added).) Another section of the specification states:

> The preparation according to the present invention exhibits marked improvements, over the conventional drugs in terms of not only ototoxicity but also tissue distribution and excellent therapeutic effects on otopathy, *particularly* otitis media and otitis externa.

(*Id.* (emphasis added).)[8] In light of the claim language

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[8] Daiichi points out that *otitis media* and *otitis externa* are the only forms of bacterial ear infections known to be susceptible to topical administration of ofloxacin. In the Court's view, that fact does not foreclose the possibility that, the term "otopathy," as used it the '741 patent, was intended to encompass more than just *otitis media* and *otitis externa*. As one treatise on patent drafting explains, "[it] is the claim drafters job to have written the claims in the application to not only cover what they attorney and the inventor client could at the time of the application prosecution have envisioned as competing products, but to cover competitive products which neither the inventor nor the attorney thought of or could even have imagined at the time . . . Faber, *supra* note 2, at § 10:1-1.

and the specification, the Court fails to see a principled basis for adopting Daiichi's proposed construction. Unfortunately, Apotex' proposed construction is no more persuasive. Apotex argues that the "plain and ordinary meaning" of the term "otopathy," and the one which the Court should adopt, is "any disease of the ear." In support of its argument, Apotex points out that during the patent prosecution process, Daiichi submitted to the PTO an excerpt from Dorland's Medical Dictionary, 26th edition, which defines "otopathy" as "any disease of the ear." (Krol Decl., Exh. I.) Apotex' argument is unconvincing for two reasons.

First, Daiichi represents to the Court that it submitted Dorland's Medical Dictionary definition of "otopathy" to the PTO only because Daiichi was required to do so pursuant to Patent Office Rule 56, 35 C.F.R. § 1.56. Specifically, the Dorland's Medical Dictionary definition had been submitted during the prosecution of the foreign counterpart to the '741 patent and, therefore, was required to be disclosed to the PTO pursuant to Daiichi's duty of good faith and candor. (Daiichi Brief in Response to Apotex' Brief on Claim Construction ("Daiichi Reply"), at 5.) In fact, the record shows that the Patent Examiner crossed the definition off of Daiichi's Form PTO-1449, indicating, as the Form PTO-1449 itself instructs, that the Patent Examiner did not rely on Dorland's Medical Dictionary in its consideration of the '741 patent application. Apotex offers nothing to rebut these facts.

The second, and perhaps more important, reason why the Court rejects Apotex' proposed construction is the recent and much-anticipated *Phillips* decision, in which the Court of Appeals for the Federal Circuit,

sitting en bane, issued a strongly worded caution against the blind use of dictionary definitions in claim construction analysis. As stated in *Phillips:*

> The main problem with elevating the dictionary to such prominence is that it focuses the inquiry on the abstract meaning of words rather than on the meaning of claim terms within the context of the patent ... *heavy reliance on the dictionary divorced from the intrinsic evidence risks transforming the meaning of the claim term to the artisan into the meaning of the term in the abstract, out of its particular context, which is its specification.*

Phillips, at 1320, 2005 WL 1620331, *14 (emphasis added). The Court of Appeals further elaborated, "there may be a disconnect between the patentee's responsibility to describe and claim his invention, and the dictionary editors' objective of aggregating all possible definitions for particular words." *Id.* This Court finds the Court of Appeals' warning in *Phillips* especially pertinent here.

Neither the Court, nor Daiichi, dispute that the term "otopathy" may be literally translated into "a disorder of the ear." That does not, however, mean that this is how the term should be construed in the context of the '741 patent Rather, viewing the disputed term from the perspective of the ordinary person skilled in the art, as this Court is required to do, precludes such an interpretation.

A pediatrician or general practitioner, let alone an otolaryngologist, would know that ofloxacin is an anti-bacterial agent whose only therapeutic purpose is to kill or eradicate bacteria. The pediatrician or general practitioner would therefore assume that the

otopathy to which the '741 patent is directed must be amenable to antibiotic treatment—that is, infections caused by the presence of bacteria.[9] Accordingly, the Court concludes that the most sensible construction of the term otopathy, as used in the '741 patent, is "bacterial ear infection."

2. "effective to treat"

[16] Daiichi argues that the phrase "effective to treat" otopathy means "safe and efficacious to treat." (Daiichi Br., at 21.) Apotex disagrees, and argues that the term "safe" should not be read into the patent claim. The Court agrees with Daiichi.

[17] It is proper to interpret terms and phrases appearing in the claim in light of the fundamental purpose and significance of the invention. *Minnesota Mining & Mfg. Co. v. Johnson & Johnson Orthopaedics, Inc.*, 976 F2d 1559 (Fed.Cir. 1992); *In re Research Corp. Techs., Inc.*, No. 97-2836, 1998 U.S. Dist. LEXIS 23150 at *12 (D.N.J. Oct 16, 1998). Doing so in this case amply supports Daiichi's argument that "[s]afety was a paramount concern of the inventors" of the '741 patent. (Daiichi Br., at 22.)

In describing the background to the invention, the patent specification recites the following:

> Conventionally employed topical preparations for treating otopathy ... have ototoxicity as side effects or therapeutic effects thereof tend to be decreased due to emergence of resistant microorganisms.

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[9] The only other drugs mentioned in the patent specification are also antibiotics, including fradiomycin, kanamycin, chloramphenicol, and cefrnenoxime. (Krill Decl., Exh. A.)

* * * *

> In order to overcome the above-described problems, the inventors have conducted extensive investigations and, as a result, have reached the present invention.
>
> * * * *
>
> Ofloxacin is of high safety. Acute toxicity (LD_{50}) of ofloxacin was found to be 5450 mg/kg (p.o.) in mice, 200 mg/kg or more (p.o.) in dogs, and from 500 to 1,000 mg/kg (p.o.) in monkeys.
>
> * * * * *
>
> The preparation according to the present invention exhibits marked improvements over the conventional drugs in terms of not only otoxicity but also tissue distribution and excellent therapeutic effects on otopathy . . .

(Krol Decl., Exh. A.) In addition, the specification describes a number of animal studies involving the ototoxie effects of topically applied ofloxacin and data concerning the drug's safety.

In light of the extensive discussion of side-effects and safety in the patent specification, the Court concludes that it is proper to construe the disputed term "effective to treat" as "efficacious and safe."[10]

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[10] In addition, at least one district court has construed the term "effective" so as to implicitly include minimization of side effects. *Purdue Pharma. L.P. v. FR. Paulding & Co.*, 48 F.Supp.2d 420. 437 (D.Del.1999). *aird*, 230 F.3d 1320 (Fed.Cir.2000) (construing "effective to treat pain" to mean "an individual patient is provided with adequate pain relief without unacceptable side effects").

3. "intratympanically injected through a puncture of the tympanic membrane"

[18] Apotex argues that term "intratympanically injected through a puncture of the tympanic membrane," as used in Claim 7 of the patent, means "introduced into the middle ear with an instrument such as a syringe." (Apotex Br., at 25.) Daiichi urges a broader interpretation, in which the term means "forced into the middle ear through a puncture of, or a tympanostomy tube within, the tympanic membrane." (Daiichi Br., at 30.) The Court agrees with Apotex' interpretation of the disputed term.

Daiichi argues that Claim 7 should be read to include, but should not to be limited to, the use of a syringe. The basis for this argument is that since the '741 patent is directed to the treatment of *otitis media* with a perforated tympanic membrane, there would be no need to use a syringe to force the antibiotic into the middle ear cavity. According to Daiichi, Claim 7 should be construed to include the instillation of ofloxacin drops into the external auditory canal, as set forth in Claim 6, which are then forced, i.e. "injected," through the ruptured tympanic membrane using a method referred to as "pumping the tragus."[11]

Noting that the language of Claims 6 and 7 does nothing to support this interpretation, the Court finds that a close reading of the patent specification precludes this Court from adopting Daiichi's proposed construction. Specifically, in several sections of the specification, "intratympanic injections" are

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[11] "Pumping the tragus" essentially means wiggling the ear so as to exert pressure on the fluid in the external auditory canal.

distinguished from the instillation of ear drops. The specification states:

> Dose forms of the topical preparation of the present invention include sprays, otic solutions, *e.g. intratympanic injections and ear* drops, ointments and the like.
>
> * * * *
>
> In administration of the ofloxacin solution, several 0.5 ml-doses per day are applied to the external auditory canal by spreading, spraying or *instillation, or intratympically injected* through a puncture of the tympanic membrane.

(Krol Decl., Exh. A. (emphasis added).) Indeed, even Daiichi's own expert, Dr. Angelo Agro, testified at her deposition, that an ordinary person skilled in the art would not have known at the time the '741 patent was issued that "intratympanically injected" meant "pumping the tragus." As Agro testified:

> Q: At the time of the invention, were any ototopical preparations being intratympanically injected in the fashion you are describing [pumping the tragus)?
> A. No.

(Krol Decl., Exh. M, Transcript of Deposition of Angelo Agro, M.D., 115:5-11.)

Had Daiichi intended the act as its own lexicographer and defined the term "intratympically injected" to mean "pumping the tragus," it was certainly free to do so by clearly defining the term in the patent specification. Having failed to do so, the Court finds that the most sensible construction of the term is, as Apotex argues, "introduced into the middle ear with an instrument such as a syringe," an

interpretation that is consistent with the generally known meaning of the word "injection."

IV CONCLUSION

For the reasons set forth in this Opinion, the Court declares that:

(1) the term "otopathy" as used in the claims of U.S. Patent No. 5,401,741 is properly construed to mean "bacterial ear infection;"

(2) the term "effective to treat" as used in the claims of U.S. Patent No. 5,401,741 is properly construed to mean "safe and efficacious to treat;" and

(3) the term "intratympanically injected through a puncture of the tympanic membrane" as used in the claims of U.S. Patent No. 5,401,741 is properly construed to mean "introduced into the middle ear with an instrument such as a syringe."

An appropriate Order follows.

ORDER

This matter having come before the Court on the motions of DAIICHI PHARMACEUTICAL CO., LTD. and DAIICHI PHARMACEUTICAL CORPORATION ("Plaintiffs") and APOTEX, INC. and APOTEX CORP. ("Defendants") to construe certain disputed claim terms in U.S. Patent No. 5,410,741 (the "741 patent"); and

The Court having considered the submissions of the parties; and

The Court having conducted a hearing pursuant to *Markman v. Westview Instr.*, 52 F.3d 967

(Fed.Cir.1995) (*en banc*), *affd*, 517 U.S. 370, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996); and

For the reasons set forth in the Opinion issued this day; and

For good cause shown;

It is on this 5th day of August 2005 ORDERED that:

(1) the term "otopathy" as used in the claims of the U.S. Patent No. 5,401,741 is properly construed to mean "bacterial ear infection;"

(2) the term "effective to treat" as used in the claims of the U.S. Patent No. 5,401,741 is properly construed to mean "safe and efficacious;" and

(3) the term "intratympanically injected through a puncture of the tympanic membrane" as used in thc claims of U.S. Patent No. 5,401,741 is properly construed to mean "introduced into the middle ear with an instrument such as a syringe."

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

Civ. No. 03-937 (WGB)

DAIICHI PHARMACEUTICAL CO., LTD. AND DAIICHI PHARMACEUTICAL CORPORATION,

Plaintiffs,

v.

APOTEX, INC. AND APOTEX CORP.,

Defendants.

ORDER

This matter having come before the Court on the motions of DAIICHI PHARMACEUTICAL CO., LTD. and DAIICHI PHARMACEUTICAL CORPORATION ("Plaintiffs") and APOTEX, INC. and APOTEX CORP. ("Defendants") to construe certain disputed claim terms in U.S. Patent No. 5,401,741 (the "741 patent"); and

The Court having considered the submissions of the parties; and

The Court having conducted a hearing pursuant to *Markman v. Westview Instr.*, 52 F.3d 967 (Fed. Cir. 1995) (en bane), *aff'd*, 517 U.S. 370 (1996); and

For the reasons set forth in the Opinion issued this day; and

For good cause shown;

It is on this 5th day of August 2005 ORDERED that:

(1) the term "otopathy" *as* used in the claims of *U.S.* Patent No. 5,401,741 is properly construed to mean "bacterial ear infection;"

(2) the teem "effective to treat as used in the claims of U.S. Patent No. 5,401,741 is properly construed to mean "safe and efficacious;" and

(3) the term "intratympanically injected through a puncture of the tympanic membrane" as used in the claims of U.S. Patent No. 5,401,741 is properly construed to mean "introduced into the middle ear with an instrument such as a syringe."

/s/WILLIAM G. BASSLER

William G. Bassler, U.S.S.D.J.

APPENDIX D

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

2006-1564

DAIICHI SANKYO CO., LTD. (formerly Known as DAIICHI PHARMACEUTICAL CO., LTD.) and DAIICHI SANKYO, INC. (formerly known as DAIICHI PHARMACEUTICAL CORPORATION),

Plaintiff-Appellees,

v.

APOTEX, INC. and APOTEX CORP.,

Defendants-Appellants.

ORDER

A combined petition for panel rehearing and for rehearing en banc having been filed by the Appellees, and a response thereto having been invited by the court and filed by the Appellants, and the petition for rehearing and response, having been referred to the panel that heard the appeal, and thereafter the petition for rehearing en banc and response having been referred to the circuit judges who are in regular active service,

UPON CONSIDERATION THEREOF, it is

ORDERED that the petition for panel rehearing be, and the same hereby is DENIED and it is further

ORDERED that the petition for rehearing en banc be, and the same hereby is, DENIED.

The mandate of the court will issue on September 18, 2007.

FOR THE COURT,
/s/ Jan Horbaly
Jan Horbaly
Clerk

Dated: 09/11/2007

cc: Robert Breisblatt
Brian P. Murphy